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THE POSTURAL INFLUENCE OF THE SYMPATHETIC NERVOUS SYSTEM.

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IN his article on "The Sympathetic and other Related Systems of Nerves" in Schäfer's Text-book of Physiology, Vol. II, 1900, Langley [26] adopted the general term "autonomic" for the contractile cells, unstriated muscle, cardiac muscle, and gland cells of the body, together with the nerve cells and fibres in connection with them. He then subdivided the autonomic nervous system into the sympathetic system consisting of the ganglia and nerves connected with the thoraco-lumbar outflow, and the cranial and sacral outflows, which may be conveniently grouped together as the parasympathetic nervous system.

The purpose of this paper is to define the physiological principle that a very general and important influence of the sympathetic system is to supply impulses which act constantly upon certain fundamental systems of organs and to maintain the posture assumed at any given time by these structures. The cerebrospinal system, the parasympathetic system, and sometimes, as in the case of the urogenitodermal system (Gaskell [20]), some fibres of the sympathetic system itself, exert an intermittent activity upon the structures under the constant influence of the sympathetic system. As will be shown, the posture of voluntary muscles, blood-vessels and certain hollow viscera, is maintained by the sympathetic innervation of these structures. These examples will be dealt with in turn.

THE POSTURAL EFFECT OF THE SYMPATHETIC INNERVATION OF VOLUNTARY MUSCLE.

The discovery of Perroncito [27] and Boeke [8] [9] of accessory nerve endings in voluntary muscles opened up a field for physiological

research [40]. De Boer [10] [11] came to the conclusion that muscle tonus was maintained by these sympathetic nerve fibres and Langelaan [24] [25] has supported this view. But as Adrian [1], in a recent review, has pointed out, "there is an important body of evidence which is directly opposed to the view that the sympathetic has anything to do with the development and the maintenance of tone." The fundamental objection levelled at the conception of de Boer is that the experimental attempts to reduce tone in decerebrate rigidity have led to very uncertain results (Dusser de Barenne [14] [15], Van Rijnberk [30], and Cobb [12]). For instance, Cobb concludes that section of the abdominal sympathetic chain in cats has no effect on decerebrate rigidity, either by preventing its development or by inhibition. Later Uyeno [41] came to a similar conclusion for the upper extremity, viz., "that neither stimulation of the stellate ganglion nor its paralysis by nicotine have any appreciable effect on decerebrate rigidity." Adrian concludes that "there is no doubt that the skeletal muscles are connected to the sympathethic system, but the sympathetic fibres are not concerned with tone." Also Walshe [38] pointed out that "de Boer's interpretation of the function of the sympathetic innervation of voluntary muscle has been confirmed by no subsequent worker and has been impugned by all who have repeated his experiments."

The work of Royle, in the course of publication in the present issue, shows consistent diminution of tone on the side on which the sympathetic innervation of the lower limb was removed in animals otherwise unoperated upon, in animals with complete transverse lesions of the spinal cord, and in animals exhibiting decerebrate rigidity. Royle adopted with advantage the procedure of producing decerebrate rigidity at an interval of some days after removal of the ganglionated sympathetic chain in the lumbar region, and it is significant that the best contrast between the two limbs after section of the midbrain was to be seen in the case of an animal in which the sympathetic chain of one side had been removed 73 days previously. The removal of the grey rami communicantes to the upper and lower limb plexuses respectively in two human patients, showing a marked condition of spastic paralysis due to an upper neurone lesion in each case, had the same effect as in the experimental animals. These results prove conclusively the relationship of the sympathetic innervation of voluntary muscles to muscle tone.

An analysis of the effect of such an operation in the decerebrate animal shows that the plastic tonus of Sherrington [32] is absent. Thus temporarily, and for a very short time, the partially denervated limb,

like the intact limb, would assume an extended position, but this position could not be maintained and the limb would fall into an abducted and flexed position under the influence of gravity. When this relaxation does occur the muscles do not tend to remain fixed in any position in which the limb may be placed, i.e., plastic tonus is absent on this side. On the intact side, on the other hand, the plastic tonic state of the limb musculature tends to fix the limbs in any position which they may take after spontaneous relaxation, or when the observer overcomes the extension by mechanical means. In the case of complete transverse lesions of the spinal cord, though the contrast is necessarily not as marked because plastic tonus even in lower animals is less constantly shown under conditions following this injury than in decerebrate rigidity, a similar result follows the removal of the sympathetic innervation of the limb musculature. In animals with an intact central nervous system voluntary resistance against pressure directed towards altering the position of the limb is less easily maintained in the case of the limb which is lacking the sympathetic nerve supply to its voluntary musculature, than on the intact side.

It is a very significant fact that the phasic contraction of voluntary muscle remains almost unimpaired after removal of their sympathetic innervation, although the limp of the normal goats operated on by Royle, which remains for a time after complete healing of the wound has taken place, probably indicates a somewhat slower and less efficient voluntary control over the limb concerned. The main disability is to maintain a position once assumed, and this disability is present whether the position is attained by voluntary activity, mechanical deformation, or as a result of reflex activity. Following the removal of the sympathetic nerves of one limb, it has already been noted that in decerebrate rigidity the position of extension characteristic of this condition may be assumed and then almost immediately lost. It is evident that this temporary extension is brought about by the somatic innervation of the muscles, which is alone intact. The action of gravity or mechanical force easily overcomes this posture, and it is not maintained as on the normal side.

Sherrington [32] has shown that muscle tone is the result of a purposive reflex action whose source is the muscle itself, the physiological purpose of which is to endow a posture on the limb concerned (Walshe [39]). It would appear from Royle's experiments that somatic reflex arcs acting differentially upon different groups of muscles determine the posture of the limb assumed, e.g., extension in the condition of

decerebrate rigidity, and that this position is then maintained by the influence of the sympathetic system. Sherrington showed that the phenomena of plastic tonus in decerebrate rigidity could not be elicited after section of the posterior nerve roots. This function therefore is also subserved by a proprioceptive reflex arc. It disappears on section of the afferent or efferent limb of the arc as shown by Sherrington's and Royle's experiments combined. It would appear that a double peripheral proprioceptive reflex system exists to subserve muscle tone. The somatic arc determines the position assumed, the sympathetic arc maintains the position once it is assumed. Section of the posterior nerve roots destroys tone altogether. If the sympathetic efferent fibres are removed, plastic tone, by means of which a position once assumed is maintained, is absent, but the tendon reflexes depending on the intactness of the somatic reflex arc remain, but in such a condition relaxation rapidly follows the contraction phase (*vide infra*), indicating the absence of plastic tone. A series of experiments on goats, still in progress, indicate that after section of the motor nerve roots in the sacral region where the grey rami may be left intact, plastic tone remains.

The term contractile tonus may be employed in contrast to plastic tonus to indicate the state of tonic contraction which has a selective action on different groups of muscles and which is dependent on the intactness of the somatic proprioceptive reflex mechanism. The term has recently been used by Langelaan [25]. He repeated de Boer's experiments on frogs, and concluded that the maintenance of plastic tonus is a function of the sympathetic innervation of voluntary muscles. In this condition the muscle is in equilibrium. Langelaan's definition of the other element of tone of normal muscle is, that when the muscle is in a state of contractile tonus it is in a condition of slight contraction. It must also be kept in mind, as already indicated from the work of Sherrington, that contractile tonus is selective in its effect, so determining the posture of the part concerned.

The experiments so far conducted throw light upon the peripheral mechanism concerned in the production of plastic and contractile tonus. Though the investigations are far from complete, clinical facts together with experimental results so far recorded point to some of the levels of activity of the central mechanism involved in the production of the two aspects of tone.

In complete transverse lesions of the spinal cord the knee-jerk may be elicited, as shown by Sherrington [33], but its relaxation is com-

plete. The normal knee-jerk possesses two elements, the initial jerk contraction and the shortening reaction secondarily induced in muscles endowed with reflex tone. This reaction consists of a definite and maintained shortening of the contracting muscle in the relaxation phase (Sherrington). This second element is absent in spinal man, for it depends on reflexes at a prespinal level. The jerk element on the other hand is dependent upon a spinal reflex arc. And as Walshe points out [37], Sherrington's researches indicate that as the animal scale is ascended the spinal component of muscle tone becomes increasingly subordinate to the prespinal. In the spinal goat Royle showed a definite loss of posture because the somatic reflexes, predominantly flexor in character, in the limb with a double innervation, failed to impose a posture against the action of gravity on the side on which the sympathetic ganglionated cord had been excised. From this it appears that the mechanism for the maintenance of posture in these animals is effective at the spinal level. Indeed after spinal transection in animals fleeting manifestations of plastic tone do occur. The decerebrate animal shows beyond doubt, however, that the prespinal centres are involved in the maintenance of plastic tone in the normal animal. In this condition the shortening reaction of the knee-jerk is clearly exhibited. It may be stated definitely, therefore, that a prespinal arc is superposed upon a spinal reflex arc in the maintenance of posture, and that the efferent mechanism of this higher arc consists of the white rami of the sympathetic nervous system. Further, a somatic prespinal reflex arc subserves contractile tonus and when these arcs are intact a selective incidence exists in higher animals on the extensor muscles of the limbs. The sympathetic prespinal arcs consequently will maintain for considerable periods the limb in the extended posture in the condition of decerebrate rigidity. When released from this posture plastic tonus will enable the limb to be maintained in any other position.

In decerebrate rigidity the corpus striatum is removed as well as the cerebral cortex, for the section of the brain passes between the superior and inferior colliculi. It is possible that the effects of decerebrate rigidity may in part be due to the removal of the influence of the corpus striatum from the prespinal centres. It is significant that muscular rigidity is the fundamental symptom of all corpus striatum lesions except Huntington's chorea. This rigidity is in all probability an expression of the removal of the influence of a controlling centre over prespinal centres subserving reflex plastic tone; that in effect the release phenomenon of Hughlings Jackson is here exhibited. It is

interesting that Ariëns Kappers [2] has pointed out that the corpus striatum develops near the frontal end of the sulcus limitans, which according to Herrick and others ends in the præoptic recess. He suggests that on these grounds this body may be of sympathetic origin. Such facts are suggestive that removal of the influence of the sympathetic system may in future be practised in special cases where marked disability has resulted from corpus striatum lesions, following for example encephalitis lethargica in young adults.

The Postural Influence of the Sympathetic Nervous System upon Blood-vessels.

In 1885 Gaskell [19] showed that the origin of the vaso-constrictor nerves was confined to white rami of the sympathetic system. Each white ramus contains such fibres; and by means of the ganglionated cord they are distributed to the vessels in all regions of the body. When the vaso-constrictor nerves are sectioned the vessels dilate, but a state of moderate contraction still remains and in a few weeks the tonus regains its former condition. For it is characteristic of involuntary muscle that it has the property of maintaining itself "in a certain degree of shortening apart from impulses from nerve centres" (Bayliss [5]). In the case of the blood-vessels it was shown as early as 1875 by Goltz, Freusberg and Gergens [21] that further dilatation of the blood-vessels than that which immediately follows removal of the vaso-constrictor influence may be produced by stimulating another set of fibres—the vaso-dilator fibres. Such fibres occur in the chorda tympani and the nervi erigentes, and, as Stricker [35] demonstrated, in the posterior sensory roots of the nerves contributing to the formation of the limb plexuses. Bayliss [4] showed that these fibres fail to degenerate when the posterior nerve roots are cut between the cord and ganglia. No dilator effect is produced, however, after removal of the ganglion. This is the "antidromic" phenomenon, so called because it is apparently due to the passage of impulses in a direction opposite to that of the sensory impulses traversing the posterior nerve root fibres. The vaso-constrictor nerves producing a tonic effect upon the muscle of the vessels are confined to the sympathetic outflow. Are the vaso-dilator nerves absent from the thoraco-lumbar region, issuing only cranially and caudally from it like the parasympathetic fibres to other involuntary musculature? It is true that "wherever we have definite knowledge of the source of fibres supplied to the vascular muscles, we find a similar

diversity of origin" (Bayliss [6]). For instance vaso-dilatation of the hind limb is obtained from the posterior roots of the nerves entering into the formation of the lumbo-sacral plexuses. Further, Bayliss shows that in the light of recent knowledge those experimental effects which have been explained on the supposition of the existence of vaso-dilator fibres in the thoraco-lumbar outflow are open to alternative explanations. A certain clinical fact points, however, to the conclusion that vaso-dilator fibres exist in the posterior nerve root of the thoraco-lumbar region of the spinal medulla. I refer to the condition of herpes zoster. The initial symptoms of this condition Krogh [22] suggests are due to dilatation of small vessels innervated by fibres from the sensory ganglion affected by the inflammatory process, which was established to be the cause of herpes by Head and Campbell. This dilatation is probably brought about by the passage of impulses along posterior root fibres to skin vessels. If this be so, vaso-dilator fibres must issue from the thoraco-lumbar region of the cord as well as from other zones. Be that as it may, it may be definitely concluded that two sets of fibres innervate arterioles, and of these the sympathetic fibres exert a tonic contractile influence on the muscle.

What has been demonstrated for arterioles may with equal truth be said of capillaries. Conclusive evidence now exists of a capillario-motor as well as an arterio-motor activity. Krogh has recently summarized the evidence on this point, in the investigation of which, with his collaborators, he has played a foremost part. He points out [22] that Beale (1860), Krimke (1884), and Glaser (1920), have demonstrated that non-medullated nerve fibres accompany capillaries. Moreover, evidence is now definitely at hand that capillaries are contractile. In 1873 Rouget [31] observed cells on the outside of the endothelial tubes of the capillaries of the hyaloid membrane of the frog's eye, and in the following year he observed such cells contracting on the living capillaries of newt larvæ. Vimtrup [36] has succeeded in fixing and staining the cells of Rouget, and has shown that every transitional stage exists between the smooth muscle cells of an arteriole and the branched cells of a capillary.

Recent investigations also make it clear that the cells of Rouget are under the influence of the sympathetic nervous system and contraction of the capillaries results from stimulation of sympathetic fibres (Krogh [22]). Further, when the sympathetic ganglia are removed the capillaries dilate. Unlike the arterioles, the capillaries may take a considerable time to regain their tone. When it is re-established, for instance, in the web of a frog after section of the nerves, regulation of the tonus is

very imperfect, states of strong contraction alternating with complete relaxation (op. cit. p. 73). It is, Krogh concludes, clear that "the muscular coat of the capillaries possesses like smooth muscle generally a definite tonus or 'posture' in the terminology of Sherrington [34] subject in the organism to nervous, hormonal, and other influences, and the diameter of the capillary is on the whole determined by the state of contraction of its muscular coat." He believes that probably every Rouget cell has a sympathetic fibre passing to it. Not only do constrictor fibres supply capillaries, but dilator fibres also. For stimulation of the posterior nerve root fibres causes dilatation of capillaries as well as of arterioles. Doi [13] obtained this effect upon stimulation of the capillaries after the arterioles had reached a maximal dilatation under the influence of acetyl-choline. The nervous mechanisms involved in capillario-motor and arterio-motor control are identical. In each case the effect of tonic innervation of the sympathetic system is subject to inhibition by vaso-dilator fibres of the posterior nerve roots. The result of this dilatation in the capillaries is the production of a reflex erythæma dependent in mammals on a complete spinal reflex (Krogh [22]. Dilatation of the arteries and arterioles leads to a greatly increased blood flow which increases heat loss and so forms an important process in temperature regulation.

When the motor nerve to a muscle is stimulated vaso-dilatation is produced within it, as Gaskell showed in 1876. Gaskell [20] was of the belief that this effect is mainly due to the acids produced, in which case a good example is provided of intermittent activity due to chemical products modifying a tonically active mechanism under the control of the nervous system. But the action of vaso-dilator fibres cannot be definitely excluded in this phenomenon. If the dilatation be due in any measure to this cause an excellent example is provided of two intermittently acting nervous mechanisms, the cerebrospinal nerves and vaso-dilator fibres, acting together to modify conditions resulting from the tonic activity of the sympathetic nervous system.

Ranson and Billingsley [29] have established the presence of a depressor centre in the extreme caudal part of the fourth ventricle, just lateral to the obex. The vaso-constrictor centre is at the apex of the ala cinerea. Fall of blood-pressure when the latter centre or its efferent path is injured shows that it is in constant activity. It has been shown (Barbour [3]) that the vasomotor centres are under the control of the heat centre of the corpus striatum. Warming reduces the body temperature and cooling of the corpus striatum increases it. This is

especially interesting in the light of Kappers' suggestion and the clinical effects on movement of lesions of the corpus striatum. For it is evidence of another sympathetic effect subserved by the corpus striatum. This effect is lost as the level of transection passes through the middle of the diencephalon.

The Postural Influence of the Sympathetic Nervous System upon Hollow Viscera.

It has long been known that certain hollow viscera receive a nerve supply from both the sympathetic and parasympathetic outflows respectively and that when this occurs the two sets of fibres are in the main antagonistic in function. In 1899 Bayliss and Starling [7] showed that excised portions of the intestine exhibit contraction above a stimulated point and relaxation below it. Whether this phenomenon may be due to a local reflex (in the myenteric plexus), or be myogenic in origin, the intestinal movements are under the control of the central nervous system in the intact animal. The sympathetic system exercises its influence on the small intestine through the splanchnic nerves and the para-sympathetic through the vagus. Stimulation of the splanchnic nerves leads to relaxation of both coats of the small intestine. Following on initial inhibition the result of stimulating the vagus is to increase the movements of the small intestine. Now Sherrington [33] has shown that the conception of posture, as illustrated by the plastic tonus of voluntary muscle, may be transferred to the smooth muscle of hollow viscera, as well as to blood-vessels, as already shown. The normal posture of a hollow viscus at any particular time is that degree of relaxation necessary to include its contents. In the case of the intestine the best example of the mechanism on which this activity depends can be seen in the sigmoid flexure of the rectum, called the "distal portion of the colon" (Elliot and Barclay Smith [17]). The descending colon is never distended, but appears to be an area of irritability rapidly transferring its contents to the sigmoid. This is in marked contrast to the "distal colon" which becomes distended by its contents. The nerve supply of the colon is received, like the small intestine, from both the sympathetic and parasympathetic nervous systems. The former consists of inferior mesenteric nerves, stimulation of which causes relaxation of the bowel and contraction of the internal sphincter of the anus. The pelvic nerves of the parasympathetic nervous system when stimulated cause evacuation by contraction of the muscle wall and relaxation of the sphincter. It will be observed that

normally evacuation is the result of an intermittent activity superposed upon a continuously acting sympathetic influence which regulates and maintains the "posture" of the bowel until the parasympathetic reflex leads to defæcation.

An excellent illustration of the continuously acting regulating effect of the sympathetic innervation of the distal colon can be obtained by transecting the spinal cord above the last thoracic level. The experiments were performed on rabbits. Immediately following the transection of the cord there is retention of fæces. It is possible to open the peritoneal cavity of a spinal animal without the administration of an anæsthetic, although light ether anæsthesia was sometimes employed. The distal colon will be found to be inactive. That this is not due to temporary reflex inhibition, a result of the incision, is shown by the overdistension exhibited by this part of the bowel due to retention of fæces since the time of operation, e.g., twenty-four hours previously. If the bowel be distended by the injection of normal saline through the anus, reflex contraction of the bowel may be elicited and the fluid extruded together with a few scybala, showing that the parasympathetic reflex is intact. Dilatation of the gut wall and contraction of the rectal sphincter when the enema is passed out replaces the temporary contraction of the wall. If the hypogastric nerves be now removed or the ganglionated sympathetic cords in the lumbar region be excised a marked change occurs. Immediately activity of the distal colon is resumed, the longitudinal muscle shortens, and the circular fibres contract and the scybala are pushed on into a relaxed portion of the gut distal to the site of contraction. Evacuation is thus accomplished.

A more localized effect may also be produced by removing only a few hypogastric nerve fibres at a time, instead of excising the ganglionated cord. This may be done by ligaturing and cutting off small sigmoid vessels and their accompanying nerves, care being taken to preserve an adequate blood supply to the gut. After each section a marked localized contraction of the gut occurs about 1 cm. distal to the junction of the vessel severed and the gut wall. Branches of the superior hæmorrhoidal vessel were treated in like manner and defæcation proceeded. In one experiment it was noted that between active segments proximally and distally, a portion of bowel 2·5 cm. in length remained greatly distended and contained seven scybala heaped up within it. Ligature and section of the nerves proceeding to this segment led to its active contraction. As the bowel emptied it remained contracted and the tæniæ formed distinct bands upon its surface.

These experiments prove that the retention of fæces in the first stage of complete transection of the spinal cord is due to a continuously acting inhibitory effect upon the distal colon brought about by a reflex arc through the hypogastric nerves; owing to the removal of impulses from higher centres the normal balance of activity between the sympathetic and parasympathetic system is lost. For instance it has been shown that stimulation of the sciatic nerve causes the defæcation reflex through the pelvic nerves, but transection of the cord at any level destroys this action, pointing to the presence of a centre in the medulla oblongata (Ranson [28]). The hypogastric nerves as a result of the loss of balance of action impose a posture upon the bowel, which enables contents to accumulate in it greatly in excess of what normally excites the reflex activity of the pelvic nerves. But when the sympathetic influence is removed the pelvic nerves hold sway.

In Royle's first patient an interesting phenomenon followed section of the lumbar white rami of the sympathetic system, of a similar nature to the experimental results obtained by removal of the hypogastric influence on the distal colon. Prior to the operation daily doses of sodii sulphas (1½ drachm) were required to obtain any action of the bowels. Following the operation the bowels have acted without aperients always once, sometimes twice, each day. The sectioning of the white rami on one side was undertaken with some trepidation lest unilateral removal of the hypogastric nerves should materially influence the bladder and rectal functions. In subsequent operations Royle intends to cut the grey rami only if the voluntary muscles alone need be operated upon; but the beneficial results obtained by sectioning the white rami and so removing the influence of the hypogastric nerves suggests that the sectioning of the latter nerves on one side may in some cases be of therapeutic value.

It is clear that the continuously acting inhibitory effect upon the muscle of the wall and the tonic contractile effect upon the internal sphincter lead to the filling of the bowel. The pelvic nerves which relax the sphincter and contract the gut wall have the effect of emptying the bowel.

The hypogastric and pelvic nerves have a similar function to perform in at least some animals in controlling the bladder, as that already described for the alimentary canal. Elliot [16] showed, for instance, that in the cat the hypogastric nerves "facilitate retention of urine" by constricting all the urethra and relaxing the bladder. The cat's bladder is a good example of this type of action because it is specialized for the

storage of large quantities of fluid. The inhibitory action in the rabbit is less widespread (Elliot), but in the experiments on rabbits detailed above, in which the cord was first transected, the greatly distended bladder emptied upon excision of the ganglionated sympathetic cords. Also Elliot concludes that "in all mammals the pelvic visceral or sacral nerves cause the whole bladder to contract: in the cat and rabbit and probably in others they also inhibit the sphincter." Elliot calls these fibres the nerves of micturition.

In general, therefore, the fundamental plan of the innervation of the bladder is the same as that of the gut. The filling nerves are supplied by the sympathetic system and the intermittently acting emptying nerves are parasympathetic in origin. In other words the "posture" of these viscera is maintained by the sympathetic nervous system. It is to be noted also that the same system regulates the posture of the blood-vessels supplying the viscera. In the filling stage the effect of the sympathetic outflow is to maintain the organ in that degree of relaxation necessary to accommodate the contents within it, and during this inactivity the vaso-constrictor nerves maintain the posture of the blood-vessels so that no increase of blood is supplied to the part. In this sense the functions of these two sets of sympathetic nerves are not antagonistic but complementary to one another.

General Summary.

If the phenomena discussed in the foregoing sections connected with the sympathetic innervation of voluntary muscles, blood-vessels including capillaries, and hollow viscera, be reviewed in conjunction with one another, the general conclusion is arrived at that in each of these systems the sympathetic influence is continuously active. In voluntary muscle it produces plastic tonus which is subject to modification by the cerebro-spinal system. The constriction of arteries, arterioles, capillaries and venules is brought about by the same influence and may be inhibited by vaso-dilator nerves. The involuntary muscle of hollow viscera is maintained in that degree of relaxation appropriate to accommodate the contents within it, and the sphincters are tonically contracted by the sympathetic innervation. The parasympathetic nerves intermittently stimulate the muscle of the wall and relax the sphincter. In each case the sympathetic system imposes a "posture," in the sense of that word employed by Sherrington, on the structures innervated by it. It is possible to conclude, therefore, that this is a general and important part of the function of the thoraco-lumbar outflow which constitutes the sympathetic nervous system.

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THE PROBLEM OF TREATMENT OF SPASTIC PARALYSIS:

An Experimental and Clinical Study.

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The problem of treatment of spastic paralysis has, so far, evaded a satisfactory solution. Procedures based upon the accepted physiology of the condition have undoubtedly improved the disabilities of patients suffering from the disease, but have not effectually removed the spastic gait nor delivered the sufferer from the wearying process involved in performing movement in the presence of muscular rigidity.

The discovery of Boeke [2] that voluntary muscles are supplied by non-medullated nerve fibres from the sympathetic system in addition to medullated fibres from the anterior horn cells, has opened a new avenue for investigation into the mechanism of the control of movement.

De Boer [4] claimed that section of the sympathetic fibres supplying the muscles of a limb produced a change in tone. Langelaan [8], accepting de Boer's results, contended that the sympathetic was concerned with the maintenance of "plastic tone" in contradistinction to the "contractile tone," depending upon the integrity of the medullated nerves. Direct stimulation of the sympathetic has failed to effect a change in muscular tone, but, if Langelaan's conception be correct, stimulation of these fibres would not cause a change in length, since their function is to maintain the existing length of a muscle.

Kuno [13] repeated many of de Boer's experiments and formed the opinion that the results obtained were due to the effects of vaso-dilatation in the limbs deprived of their sympathetic supply, But a much more important objection to the theory is that, according to the experiments of Dusser de Barenne [6] [7], Van Rijnberk [11] and Cobb [3], section of the sympathetic fails to influence the development and maintenance of decerebrate rigidity. This condition is generally admitted to be due to a great increase in the tone of the muscles maintaining the animal against the effect of gravity, and if the sympathetic nerves have

anything to do with tone the effect of their removal should be noticeable in this condition. These three investigators carried out experiments on cats by destroying the abdominal sympathetic trunk on one side either before or after decerebration. Dusser de Barenne found a diminution in tone in five cases out of nine; van Rijnberk could detect no constant difference in nineteen experiments, and Cobb found none in a series of six.

Similar experiments are reported by K. Uyeno [10], who failed to notice any appreciable difference in the rigidity of the forelimbs in a decerebrate animal when the stellate ganglion was stimulated electrically, paralysed by nicotine or completely removed.

Langelaan [9] has recently repeated de Boer's experiments and while he has demonstrated marked changes following sympathetectomy in the hindlimb of the frog under certain conditions, he has not shown that these changes are present in a decerebrate animal.

Adrian [1] in reviewing all the evidence on the question comes to the conclusion that all the recognized phenomena of tone can be produced in muscles which have been deprived of their sympathetic supply, and that the only reason for supposing that the sympathetic fibres have any function at all is the fact that they exist. In a later article this view is supported by F. M. R. Walshe [12].

Experiments to determine the Function of Sympathetic Nerves supplying Voluntary Muscles.

In the light of the above reviews it is obvious that the function of the sympathetic fibres going to voluntary muscles has not been definitely determined. Experiments were therefore carried out to determine:—

(1) What the function of the sympathetic fibres was.

(2) Whether that function had any relationship to the phenomena of spastic paralysis. Actually the whole research was carried out with a view to finding a method of dealing with the rigidity in spastic paralysis, and the undetermined function of the sympathetic fibres supplying voluntary muscles afforded a field for investigation.

Series I.

The following experiments were done:—

To increase the tone in the muscles of the lower limb the spinal cord of a rabbit was completely divided in the thoracic region. The left abdominal sympathetic trunk was removed immediately after the

section of the cord. Within a short time it was evident that there was a decided difference between the left and the right lower limbs. When the animal was suspended the right lower limb was maintained in a flexed attitude, while the left one hung in an extended position. There was also a decided difference in the amplitude of the knee-jerks; on the left a normal response was obtained, while in the right percussion of the patella tendon led to an exaggerated extension of the leg. Attempts to reproduce this experiment gave unsatisfactory and inconsistent results. It is not altogether easy to be sure about the complete removal of the sympathetic on one side and on one side only in the rabbit, and in so small an animal changes could occur which might escape observation. It was therefore decided to use a larger animal with a more definite sympathetic trunk. In all subsequent experiments the goat was used.

Goat I (1).—The spinal cord was divided on May 30, 1923. Two days later the left abdominal sympathetic trunk with its communications was removed. This was followed by an immediate change in posture in the left lower limb. When the animal was placed on its back the left lower limb was a little more extended and a little more abducted than the right. On the third day the right lower limb was maintained in flexion and adduction; the left was extended and was abducted at the hip. The knee- and ankle-jerks on the right were exaggerated and the limb returned to the flexed attitude after elicitation of the knee-jerk. In the left limb knee- and ankle-jerks were obtained but were of a normal type, and when the left lower limb was placed in the flexed attitude elicitation of the knee-jerk was not followed by a return to the flexed attitude but the limb remained extended. On the fourteenth day the right lower limb was still spastic in a flexed position. The left lower limb could be moved passively without any noticeable resistance.

Passive extension of the right lower limb was followed by two or three movements of flexion, while extension of the left lower limb resulted in only a slight degree of adduction of the thigh. When both lower limbs were extended simultaneously the right was immediately drawn into the flexed attitude, but the left remained extended. On the sixteenth day the knee- and ankle-jerks became more marked on the left, while there was actually a decrease in the reflex activity in the right lower limb. On the following day the reflex activity was still more marked on the left side. On the twenty-first day the reflexes were still active on the left but had practically disappeared on the right

side. The animal died on June 22, 1923, with the condition practically unaltered. The alteration in the relative conditions of the two lower limbs which occurred within sixteen days after the section of the sympathetic was due to some degenerative change occurring in the spinal cord, and the observations after this time did not give a reliable picture of the changes which occur as a result of section of the sympathetic nerves.

Goat I (2).—In this animal the left sympathetic trunk was removed on June 6, 1923, and transverse section of the cord was performed immediately afterwards. On the following day the left limb was in extension and abduction, while the right one was in flexion and adduction. The loss of posture was not as marked as in Goat I (1). There appeared to be some degree of spasticity in the flexors of the thigh on the fifth day, but there was a marked extension of the ankle-joint in contrast to the flexed condition on the right side. Eight days after the operation was performed the animal did not appear to be well. The posture of both lower limbs was similar as regards the position of the hip-joint, but the ankle and the foot were much less flexed on the left side. No further observations were made on this animal, which died within a few days.

Goat I (3).—In this animal hemisection of the spinal cord was performed on the left side and the left abdominal sympathetic trunk was removed June 14, 1923. On the following day the right limb was in the flexed posture, the left one was extended and abducted, but the tendon reflexes were similar on each side. At the end of seven days the animal could not stand on its hind limbs, but had some voluntary control on the right side. The left lower limb did not show any marked signs of spasticity. At the end of fourteen days the animal could walk but had foot-drop on the left side. This gradually improved and almost complete recovery of function in this limb had occurred three months later, September 14, 1923. The animal ran and walked well. The left limb was not spastic, and when the animal was placed on its back it fell into abduction and semiflexion in contrast to the right lower limb, which was held extended as in a normal animal.

Series II.

In this series the effect of dividing the left sympathetic abdominal trunk without any other procedure was tried.

Goat II (1).—The operation was done on June 4, 1923, and the animal was able to walk with a limp on the following day. Three days

after operation the animal still had a limp and the limb appeared wasted. This may have been due to the fact that the muscles were softer than on the normal side. On the seventh day the animal still walked with a limp, and on placing the animal on its back it was found that the extended position of the left lower limb could not be maintained, in contrast to the right side in which the animal could keep up a firm resistance to the passive movements. There was, in addition, in the left limb an irregular coarse tremor. Eight days after the operation the animal still walked with a limp but could run. When the animal was placed on its back the right limb was held in extension, the left limb lay in the flexed position and was markedly flaccid. On the eleventh day after the operation the animal could run vigorously. When the animal was placed on its back both lower limbs were extended and it was found that the left limb could resist passive movements without evidence of tremor. When both limbs were flexed the left one fell away from the flexed position. This occurred gradually in definite jerky movements from position to position until complete extension was reached. The tendon reflexes appeared to be of similar amplitude on each side. Fifteen days ofter operation the animal still walked well and when placed on its back with both lower limbs flexed the right limb quickly extended. Occasionally the left one extended also, but the extension was never complete nor well maintained. Eighteen days after operation the animal was in good condition and the reflexes on both lower limbs were equal in amplitude. When the animal was placed on its back the left lower limb fell away from the extended position as soon as the animal was quiet. If the animal was frightened both lower limbs extended again. This animal was kept for six weeks, at the end of which it met its death by misadventure.

Similar observations were made on all animals used in the next series of experiments. In one instance the observations extended over a period of eighty days.

Series III.

The Effect of Division of the Sympathetic Nerves upon Decerebrate Rigidity.

In this series of experiments the sympathetic trunk was removed at the first operation and the animal was allowed to recover from the effects of the surgical interference before decerebration was carried out. In this way also any sensory disturbance set up by the wound in the lumbar region was avoided. The handling of the tissues in this region

may profoundly affect reflex activity, and changes within the following few days could not necessarily be ascribed to removal of the sympathetic trunk.

Goat III (1).—The abdominal sympathetic trunk was removed on July 3, 1923. The animal made a complete recovery and fourteen days later decerebration was carried out. The anæsthetic was administered by the intratracheal method and the carotid arteries were ligated as a preliminary. The brain was then exposed and the cerebral cortex removed. This was followed by an increase in tone in both lower limbs, but the right one offered much more resistance to passive flexion than the left. This slight increase in tone was transient only. The basal nuclei and sufficient of the mesencephalon were then removed to produce decerebrate rigidity. In the right lower limb the rigidity was so marked that the limb could resist the most strenuous efforts at passive flexion; on the left side, however, although extension occurred, the condition was much more easily relaxed. In the intervals, when rigidity of the lower limbs was less marked, striking differences were noticed. If both lower limbs were extended and abducted simultaneously and then released together the left fell immediately into a completely flexed position, while the right one fell slowly and finally assumed a very much less flexed attitude. When the knee-jerks were tested in these positions a marked response was obtained on the right side; on the left the knee-jerk was not more active than that obtained in a normal animal in repose. These differences are still more marked twenty hours after decerebration. The animal lived for about twenty-one hours after the operation had been performed.

Goat III (2).—The left abdominal sympathetic trunk was removed on July 24, 1923. Decerebration was carried out at the end of fifteen days. At the time of this second operation the animal was not well, and when the trachea was opened it was found to be filled with mucus. The animal died shortly after the operation. Decerebrate rigidity developed with the difference on the two sides that has been already described in the account of the first experiment of this series.

Goat III (3)—The left abdominal sympathetic trunk was removed on July 31, 1923. Following the operation there was less reflex activity in the left leg and the same inability to maintain a posture when the animal was placed on its back. Eight days later decerebration was performed. When decerebrate rigidity appeared it could be very much more easily relaxed on the left side than on the right, though in this animal, both in the forelimb and in the hindlimb of the right side,

there was less rigidity than in previous experiments. When both hindlimbs were extended into the perpendicular position with the animal lying on its back the left limb quickly fell into abduction, while the right limb maintained the perpendicular position. On the following day the animal was still alive, and the hindlimbs showed similar differences, though the rigidity of the right forelimb was still less marked than that in the left.

Goat III (4).—This animal had the left abdominal sympathetic trunk removed seventy-three days before decerebration. When decerebrate rigidity appeared the left lower limb extended for a few seconds only and then fell into flexion and remained flexed while the other three limbs remained rigidly extended.

In this animal it was quite clear that although the tendency to extension of the limbs affected the left lower limb, decerebrate rigidity as described by Sherrington did not appear. Shortening and lengthening reactions were well shown in all limbs except the left lower limb, whose position was determined by gravity. This limb exhibited also a decreased but definite tonic condition. The knee-jerk was obtainable, but not as readily as in a normal animal. When the left lower limb went into extension the contrast in the two lower limbs was remarkable. The greatest force had to be employed to overcome the rigidity in the right limb while in the left the absence of rigidity enabled flexion to be easily effected. A moving picture record of this animal was taken on the day following decerebration and illustrates this point clearly.

Comments on Results.

It will be seen in examining the details of these experiments that section of the left sympathetic abdominal trunk produced similar changes in every experiment. Simple removal of the left abdominal sympathetic trunk without any other procedure did not interfere with the animal's ability to control the left lower limb, but the animal was certainly not able to maintain the limb in the extended position when placed on its back, and the amplitude of reflex movements was diminished. Similar observations to those described in Series II were made on five other animals. In every case the observations indicated that there was certainly a definite change in the left lower limb when compared with the normal limb of the opposite side, and that change may be described as a depression in reflex activity and an inability to maintain the posture of the limb. In transverse section of the cord when the reflex activity of both lower limbs is increased, section of the left

abdominal sympathetic trunk led to a very marked alteration in posture of the left lower limb. The right lower limb was held in the flexed attitude, and there was a marked increase in the reflex activity of the limb. The left lower limb fell into abduction and extension, and while the knee- and ankle-jerks could be obtained the amplitude was not as great as on the right side. When decerebrate rigidity was produced under the conditions which have been described in Series III, marked differences between the left and the right lower limbs were still evident. The division of the left abdominal sympathetic trunk prevented the onset of decerebrate rigidity in the left lower limb, but the limb participated in the periodic extending movements only to fall into flexion immediately. The extension could be easily overcome in the left limb, while in the right the greatest force had to be used to place the limb in flexion.

During the intervals when the rigidity was less marked the right and left lower limbs still exhibited a striking contrast. The knee-jerk on the right side was very easily obtained and was exaggerated. On the left side the knee-jerk was not easily obtained, and there was not always a response to percussion of the patella tendon. When the movement did occur the amplitude was not nearly as great as on the right side, and the limb immediately fell back into the flexed attitude. The right limb, on the other hand, usually maintained a semi-flexed attitude through the period of decerebration. Conditions were most marked in the fourth animal, and it appears that the length of time between the removal of the sympathetic trunk and decerebration is a factor which alters the character of the observations. The least striking changes were seen in animal III (3), and the most striking in animal III (4), which was decerebrated seventy-three days after removal of the sympathetic nerves. The differences in the reflex activity in the lower limbs of these decerebrate animals were very marked and the amplitude of the knee-jerk appeared to be influenced by the position in which the reflex was effected. In the position of semi-flexion the right lower limb gave a vigorous response, while in the left lower limb the position of complete flexion and the relative flaccidity of the limb led to a much smaller response. When the left lower limb was placed in a position of semi-flexion a vigorous response could be obtained in it also. The difference in these two limbs was thus to be expressed as a difference of posture. The right one tended to maintain a position of semi-flexion against the action of gravity, while the position of the left one was determined by gravity.

Experimental Operation and Changes following in Human Subject.

The differences in all these animals were so marked and so consistent that it was considered justifiable to test the therapeutic value of the observation and endeavour to find some relief for the rigidity accompanying spastic paralysis in the human subject. A willing patient, A. C., was obtained and submitted to operation on September 1, 1923. This patient had a gunshot wound of the cerebral cortex. The bullet had entered his skull just above the left ear and caused an extensive laceration of the cerebral hemispheres in the region of the central sulcus of the left side and had extended across the middle line on to the opposite cerebral hemisphere. The patient at time of the operation was aged 30, and the injury had been received seven years previously. He could not speak for three months and was unable to walk at all for over two years after the receipt of the injury. Spastic hemiplegia was present on the right side of the body and the left limb was affected also, but only in the leg and foot. The knee-jerk of the left lower limb was normal, the ankle-jerk was exaggerated and there was an ankle clonus. The whole foot was rigid and the patient's control was very defective. The only deformity present on the left side was a slight degree of talipes equinus. On the right side there was an exaggerated knee-jerk, a patellar clonus, an ankle clonus and an increase in the ankle-jerk. The patient could walk but had the greatest difficulty in controlling the right lower limb which he moved as one rigid piece. When he placed weight on the limb there appeared a coarse uncontrollable tremor. He could not stand on the right lower limb, though he could stand comfortably on the left. It was only possible for him to move forwards; lateral or backward walking could not be carried out. There was present only a slight degree of talipes equinus on the right side. This patient was subject to occasional tonic fits of only short duration, and which could be easily controlled by the administration of sedatives. The control of his genito-urinary system was normal, but the patient suffered from chronic constipation.

The operation.—An incision was made to the lateral side of the right sacro-spinalis muscle and extended from the last rib to the crest of the ilium and forwards for about 3 in. The lumbo-dorsal fascia was divided at the lateral side of the sacro-spinalis and the oblique muscles were freed from the crest of the ilium for about 2 in. The left hand was then passed behind the peritoneum and in front of the fascia covering the quadratus lumborum and the psoas muscles until the vertebral column was reached. The abdominal wall and the abdominal

contents were then retracted forwards and the right sympathetic trunk was exposed. There is some difficulty in doing this owing to the depth of the wound. In a normal adult the distance from the line of incision to the abdominal sympathetic trunk is between 6 and 7 in., and difficulty was experienced in getting dissectors of sufficient length to carry out the necessary blunt dissection in the region of the sympathetic trunk. The trunk lies conveniently in an anterior position on the lumbar vessels, but is overlapped by the inferior vena cava which had to be gently pushed aside. The sympathetic trunk was not difficult to recognize in the living subject, but had actually a very different appearance to that seen in the cadaver. One surprising feature was the number and complexity of the branches. The trunk was exposed from the second lumbar to where it disappeared under the iliac vein. The white ramus from the second lumbar nerve was first divided and the grey rami going to the second, third and fourth lumbar nerves were avulsed. The fourth lumbar ganglion was then defined and the sympathetic trunk was divided immediately below. By this means the grey rami communicantes to the fifth lumbar nerve and to the sacral nerves were divided.

Following the operation the patient had very little discomfort and no evident alteration of the functions of the bladder and of the rectum. On the first day the patient had $\frac{1}{6}$ gr. of morphia only and described his own condition as comfortable. Six hours after the operation the patient was examined. The right lower limb felt warmer than the left, but there was actually no difference in temperature to be detected with an ordinary clinical thermometer. The right lower limb was a brighter colour than the left and there was evidence of capillary dilatation. There was no swelling, but on measuring the circumference of the calf the right was about 1 cm. larger than the left. The muscles of the right lower limb were also undergoing coarse fasciculation which disappeared when the muscles were completely relaxed. This was particularly noticeable in the calf muscles. On comparing the right leg and foot with the left there was a marked contrast in the spastic condition. If the left foot were passively pushed into dorsiflexion there was a tendency for this position to be maintained and the attitude was only slowly relaxed. On the right side, however, passive dorsiflexion of the foot was followed by immediate and complete relaxation. The knee-jerk was still exaggerated and an ankle-clonus could still be obtained. The patient felt that in the right lower limb a great change had occurred which he described as a feeling of freedom. On the day

following the operation the control of the right lower limb had improved. Fasciculation was still evident in the calf muscles. There was still no swelling, but the limb felt warmer and was a deeper shade of pink than the opposite limb. This colour did not disappear with pressure. The patient bent and straightened his knee easily, the passive movements of the foot and ankle were easily done in marked contrast to the rigidity which still obtained in the left leg and foot. There was no disturbance in the control of the bladder. Two days after the operation the patient was still comfortable, the reflexes on the right side were still exaggerated, but the patient discovered that he could move the right lower limb as easily as he could the left. Fasciculation was still evident in the calf muscles and for the first time was noticed in the extensors of the toes. The limb still had a more flushed appearance than the opposite one. On the fourth day following operation the reflexes were exaggerated on the right side, though there was no return of rigidity. Fasciculation in the calf muscles was apparent. On the fifth day the fasciculation appeared to be less marked. The reflexes were still increased, but there was less tendency to clonus in the right lower limb. On the seventh day fasciculation had almost disappeared. The other conditions remained practically the same.

During the whole period the patient had very little discomfort and was able to stand on the ninth day. It was then found that the tremor which previously had appeared when he tried to use the limb was not present. He could walk one or two steps when supported, and expressed the opinion that he had regained control of his limb. On this day fasciculation could hardly be detected and the ankle-clonus was less easily elicited. On the tenth day after operation the patient could stand easily and walk a few steps. The control of the right lower limb was so much improved that the patient could hold the limb extended while a slipper was put on his foot. On the twelfth day following operation the patient's attempt to walk was characterized by movements which were exaggerated in amplitude. This tendency was due to his previous habits and on being corrected a fair attempt at walking was carried out. In addition he was able to walk backwards for the first time since his injury. Fasciculation was no longer detected. The colour of the right lower limb was still brighter than that of the left, and on removing pressure the colour took about twice as long to return on the left as on the right. The patient was allowed to sit up on the fourteenth day and carry out short periods of walking exercises. When examined on the

seventeenth day the patient walked with great improvement in his movements. He was able to walk backwards almost as well as forwards, and could balance his weight on the right lower limb when using a stick in the opposite hand. There was some degree of fasciculation seen in the calf muscles after walking. The vasomotor disturbance had practically disappeared and there was no difference in the rate of return of colour after pressure in either limb. On the nineteenth day after operation the patient had so far improved as to be able to walk up and down steps, using each limb alternately to negotiate each step.

On the twenty-fourth day after operation further improvement had occurred. There was practically no clonus in the right ankle, though this condition was still marked on the left side. The patient could easily ascend and descend a flight of steps, but during the descent it was noticed that when the whole weight was taken on the right lower limb a slight tremor appeared. This did not interfere with the actual control of the movements.

Thirty days after operation the knee- and ankle-clonus had disappeared on the right side; ankle-clonus was still present on the left. There was actually very little difference between the amplitude of the knee-jerks of the two sides. The patient had now acquired the ability to relax the right lower limb during the phase of movements when weight was taken on the left lower limb, and to carry it forward in a manner closely approximating to the normal gait. Walking up and down stairs was also performed quite easily. The right lower limb was still slightly larger than the left but the difference in circumference did not amount to more than 0·5 of a centimetre. There was no difference in colour and the capillary circulation could be obliterated with equal ease on both sides. On the forty-second day following operation improvement in control of the right lower limb was still continuing. Although the patient walked comparatively easily he had not yet established control over the groups of muscles in his right lower limb. He could extend his knee-joint, but had very little idea of performing flexion of the knee or any of the movements at the ankle-joint or of the foot. The control of his hip muscles was fairly well established and the patient could carry out movements in all directions but within certain limits. It was then noticed that the range of movement in the various movements at the hip-joint was still limited by a certain amount of structural shortening which had occurred in the abductors of the thigh. There was also still a definite amount of equinus deformity present at the ankle-joint which prevented the patient from clearing the ground

in a normal fashion. This deformity was due to structural changes as there was actually present a contracture in the plantar-flexing muscles.

Fifty-four days after operation the patient had improved to such an extent that he relaxed the formerly spastic limb almost in a normal manner when walking. The knee-jerks were practically equal on both sides, but with regard to the ankle-clonus it was still present in a marked form on the left side but was not present on the right side, nor was there any sign of abnormal tone in the muscles of the right lower limb.

Second patient.—Patient, H. C., had suffered from spastic hemiplegia on the right side for fourteen years. The upper limb was useless as there was only the slightest degree of voluntary control in the flexor profundus of the fingers. The hand was rigidly dorsiflexed at the wrist, flexed at the metacarpophalangeal joints, extended at the proximal interphalangeal joints and flexed at the distal interphalangeal joints. The thumb was dorsiflexed at the metacarpophalangeal joint and flexed at the interphalangeal joint. The forearm was fixed in pronation and could not be passively supinated. The rigidity was so marked that it was impossible to flex or extend a finger passively, and the extensors of the wrist resisted forceful passive flexion. The wrist-jerk was exaggerated and was followed by a clonus.

The operation.—The operation was performed on October 17, 1923. An incision along the posterior border of the right sterno-mastoid muscle gave access to the brachial plexus. The nerve roots were exposed and traced to their origin behind the scalenus anterior muscle. The scalenus anterior was lifted forwards and the rami communicantes to the fifth, sixth and seventh cervical nerves were defined. The rami to the eighth nerve and the first thoracic nerve were obtained by carrying the dissection downwards behind the subclavian artery. The grey rami to the whole plexus were then avulsed and the wound closed. This approach avoids all important structures in the neck and allows the essential operation to be carried out, that is to divide the efferent sympathetic fibres to the musculature of the upper limb.

Changes following the operation.—Immediately after the operation it was evident that the former rigidity had been very much diminished. It was possible to flex passively the wrist without any resistance from the extensor muscles. The fingers could be flexed and extended at the interphalangeal joints, but could not be extended at the metacarpo-phalangeal joints on account of structural changes which had occurred

there. The forearm could be supinated without resistance through an angle of about 45°. The following day the patient discovered he could voluntarily dorsiflex the wrist-joint and three days later he could supinate his forearm. The reflex activity was very much diminished though the wrist-jerk was still easily elicited. Vasomotor disturbance similar in character to those described in the patient A. C. was observed.

Since the operation there has been a remarkable gain in voluntary control in this perfectly useless hand, and there appears no reason why improvement should not continue when the structural deformities become less marked. The patient underwent operation only fourteen days before this account was written.

Changes in the Human Subject following Division of the Sympathetic Nerve.

(1) A remarkable change has occurred in the function of the lower bowel in the patient A. C. who underwent the operation described above. Before the operation it was necessary for the patient to take large doses of purgatives every day. Since the operation constipation has entirely disappeared and there has been no necessity for the administration of any purgative at all. According to the patient's description the movements of the bowels are normal and a motion occurs at least once daily.

(2) The most outstanding change that has occurred in these patients is the diminution of rigidity. In each case there is also a diminution of the amplitude of reflex movements. The diminution of rigidity has restored the patient's balance on the affected limb in one case, and has enabled the patients to be able to relax voluntarily the affected muscles in both cases. The loss of balance in spastic paralysis appears to be due to the fact that the patient cannot quickly change position. With the diminution of rigidity the change of position is easily effected and alterations in the centre of gravity can be compensated by changes in the state of contraction of the muscles of the lower limb. The tremor which was such a marked feature of the patient's (A. C.) right lower limb before operation has entirely disappeared. Before operation this was so marked that the patient could not maintain his weight on this limb. The probable explanation of the disappearance of tremor again depends upon the diminution of rigidity.

(3) There was in both these patients an immediate and progressive gain in control. In the patient A. C., the only movement that

could be performed as an isolated action was extension of the knee. Since the operation flexion and extension of the hip-joint, adduction and abduction at the hip, dorsiflexion and plantar flexion of the ankle-joint have been definitely acquired. The mental effort required in performing movements is very much less, and the patient's concern now is to try and co-ordinate the various movements of progression and not simply to lurch forward on a rigid limb.

(4) The vasomotor disturbances in both of these limbs were only marked during the first week following operation. The changes were characterized by an alteration in colour of the limbs, by inability to obliterate the capillary bed, and apparently by a slight increase in the size of the limb. Unfortunately the patient's limbs were not measured before operation, but following operation in the case of the patient A. C. there was never at any time more than 1 cm. difference in the circumference of the calf muscles. At the end of a fortnight these changes had practically disappeared. The patients have had no discomfort from vasomotor changes, and have been quite unconscious that any such changes have occurred. Hartman, Blatz and Kilborn [7] have shown experimentally that the increase in volume and temperature in a limb deprived of its whole nerve supply is only transient in nature.

(5) An important question that had to be decided before the sympathetic nerves were cut, was whether there would be any wasting following operation. In the case of experimental animals the difference in weight of the tibialis anterior and the extensor communis digitorum for a period exceeding twenty-one days did not exceed the normal variation which could occur in limbs of opposite sides in the same animal. In one case there was 4·3 per cent. difference in weight, and in another case 0·32 per cent. difference in weight. In the animal III (4), the difference in weight after seventy-three days did not exceed 5 per cent., and the normal limb was the lighter. In the case of the human subject there does not appear to be any wasting of the muscles, and the actual size of the limb in which the sympathetic nerves have been cut is slighly greater than the opposite limb.

The Application of Sympathetic Ramisectomy.

In the two patients who have submitted to operation the spastic paralysis was present in the worst conceivable form. In the patient A. C., there was practically no control of the lower limb in respect to individual movements of joints. The whole limb was rigid in extension

and the patient walked upon it as upon a rigid support. In the patient H. C. spastic paralysis had been present in the right upper limb for over fourteen years, and before operation the wrist and hand were practically rigid. There was just the slightest element of control in the flexors of the fingers. The patient had no power of pronating and supinating movements. In both of these instances there has been a remarkable diminution of rigidity with such an increase of the ability to control movements that the procedure should be effective in practically all cases of spastic paraplegia and hemiplegia. It is of course reasonable to suppose that the best results will be obtained in those patients who have a fair cortical representation of individual movements. In spastic paraplegia of infancy the difficulties of balance would be very much lessened after section of the sympathetic nerves. In addition the diminution of rigidity would enable the patient to make effective whatever cerebral control happened to be present and should assist materially the process of education. In those instances where hemiplegia comes on as the result of trauma or disease and the paralysis is not progressive in nature, similar results should be obtained, in all probability much more readily as in these cases the process will be one of re-education only.

Modification of Operative Procedure.

The operation which is described for dealing with spastic paralysis of the lower limb could be modified in this respect. There is actually no need to take out the white ramus from the second lumbar nerve if it is simply desired to attack rigidity in the lower limb. In this instance the division of the white ramus had an effect which was not anticipated but which indicates a possible line of treatment for chronic inactivity of the lower bowel.

In conclusion I wish to express my indebtedness to Professor John I. Hunter for his assistance in arranging the plan of experiments, and for his constant advice and help in interpreting the results obtained. He also rendered invaluable assistance in planning the surgical operations.

The experimental work was carried out in Professor Hunter's laboratories and the cost of the research was defrayed by the Department of Anatomy, University of Sydney.

Dr. John Hoets also materially assisted in the success of the research in placing at my disposal his time and skill as an anæsthetist

both for the animal experiments and in the case of the human subjects. In performing the first operation I had also the valuable moral and surgical support of Dr. T. W. Lipscombe.

Addendum.

Since the above paper was sent in for publication a further communication from the author indicates that he has now carried out his operation of "sympathetic ramisectomy" in about sixty cases.

Amongst these were cases such as the following: Hemiplegia of infancy of children of 4 and of 9 years, where the operation was for relief of the upper extremity; a case of traumatic spinal injury involving the lower extremity; a case of syringomyelia where the object of operation was to obtain relaxation of the lower limbs allowing of the assumption of the sitting posture; a case of infantile diplegia in which both lower extremities were dealt with by operation.

The author (in litt.) thus summarizes his experience so far: "I can confidently say that the results have been consistent, but that there are limitations to the value of the new procedure. Speaking generally the main indication for operation is excessive plastic tone; and again, speaking generally, the main contra-indication is the absence of cortical control. From this you can see that a complete lesion in the interal capsule, or a more or less complete lesion in lateral sclerosis or trauma of the spinal cord, will not be appreciably improved as regards function by taking out the excessive plastic element in the hypertonic muscles. We cannot expect a return of function when the cortico-spinal paths are obliterated. In patients suffering with the paraplegias and hemiplegias of infancy, where the lesion is more or less confined to the cortex, excellent results are obtained. And the same applies to traumatic lesions of the cortex."

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THE EXPERIMENTAL PRODUCTION OF RIGIDITY, OF ABNORMAL INVOLUNTARY MOVEMENTS AND OF ABNORMAL STATES OF CONSCIOUSNESS IN MAN.[1]

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[1] The greater part of this study was made in the Montefiore Hospital. I take this opportunity to express my gratitude to Dr. S. P. Goodhart, Chief of the Neurological Service, and to the resident physicians for the facilities and the assistance generously rendered.

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I.—Introduction.

In the study of problems presented by abnormal neuro-muscular phenomena, a procedure which enables the investigator to produce these temporarily at will in the human subject without any ill effects, must be of value in a number of ways. Such a procedure is the induction of sustained or intermittent muscular spasms and of abnormal states of consciousness by means of voluntary deep breathing.

The study of the neuro-muscular phenomena brought about by hyperpnœa derives greater significance from the fact that the experiments may be performed with impunity on persons afflicted with different disorders of the nervous system. An investigation of the effects of hyperpnœa on such persons has brought to light a number of new facts. It will appear, however, that only some of these facts have so far proved of assistance in the elucidation of structure and function in the nervous system. That certain of the segments of the limbs should become adducted in some cases and abducted in others, hyperextended in some cases and wholly or partially flexed in others; that one person should complain of a sense of dizziness and numbness, that another should exhibit a profound loss of power of attention, while still another should begin to roar and rave like a maniac—are phenomena which we are unable to interpret at present in intelligible terms of structure and of function.

Moreover, the very multiplicity and bewildering variety of the neuro-muscular phenomena produced by the experiments is pregnant with promise. Numerous as are the differences of the manifestations of hyperpnœa in persons with different affections of the nervous system, they are not only constant in the same person under the same conditions, but are similar in different persons suffering from similar defects. It is, therefore, not unreasonable to hope that with the accumulation of a sufficient stock of facts the procedure may prove to be of assistance in the diagnosis and localization of diseases of the nervous system, as may be partly surmised from the following examples:—

Case 1.—G. S., a man aged 26, weighing 135 lb., complained of convulsive attacks of his left upper limb.

Neurological examination revealed a doubtful inequality of the tendon reflexes on the two sides, those on the left being perhaps slightly brisker. As none of the attendants had observed any attack in this patient diagnosis was suspended.

The patient was subjected to voluntary hyperpnœa. Eight minutes after the beginning of the experiment the left upper limb was suddenly thrown into a violent spasm. Notwithstanding the fact that the duration of the seizure was only about thirty seconds, the posture produced, the violence of the muscular contractions, the oscillatory movements of the limb, and the patient's conscious state could be thoroughly observed under favourable circumstances. The patient was photographed on two successive occasions. One of the photographs, made by rapid flashlight exposure in order to eliminate the vibratory movement, is reproduced in fig. 1, making a description of the muscular pattern of the convulsed limb superfluous.

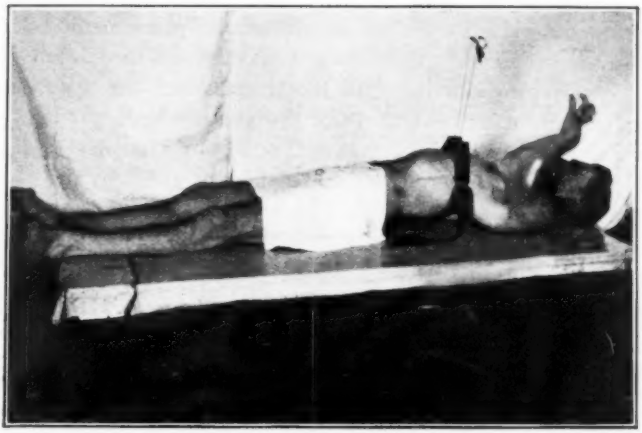


FIG. 1.—An attack of Jacksonian epilepsy induced by means of hyperpnœa. Note the intensity of the muscular contractions.

Case 2.—J. S., a man aged 28, weighing 185 lb., complained of headaches and of an uncontrollable desire to change frequently his place of employment.

A neurological examination of this patient revealed nothing definitely abnormal. He was sufficiently alert to be able to conceal his true mental condition from the examiner. His wife, however, maintained that he was suffering from ideas of persecution, and that his behaviour in private life was that of a demented person.

The patient co-operated in the experiment of hyperpnœa, with the following results :—

At the end of five minutes it was no longer possible for him to maintain the

rate and depth of respirations in rhythm with the instruments. No amount of urging availed to sustain his attention. He began to rave and roar like a wounded animal, then to laugh foolishly. He became utterly disoriented and insensible to questions and requests. Hyperpnœa was, of course, automatically discontinued. In two or three minutes, when the patient had completely recovered, he was requested to resume the exercise, which he did. At the end of five minutes, however, he once more lapsed into a state of acute dementia.

Asked subsequently to account for his peculiar behaviour during the exercise he replied simply that he could not help it.

There are few drugs the effects of which upon the neuro-muscular system are so rapid and so striking as are the effects of voluntary hyperpnœa. The administration in sufficient quantity of a drug, the action of which is to produce within a few minutes an extreme degree of muscular rigidity, must place the life of the subject in imminent danger. Yet the writer has induced such degrees of muscular rigidity repeatedly by means of voluntary hyperpnœa without the least ill effects. No matter how severe or widespread the neuro-muscular phenomena induced, no sooner is the respiratory musculature affected by the rigidity, or the state of consciousness reduced to the point when the person loses his power of attention or control, than the cause which produced these phenomena is automatically removed, and the phenomena disappear rapidly. The rate of the pulse is somewhat increased by the procedure but there is no increase in the blood pressure. No fear may therefore be entertained in experimenting upon patients who have sustained a cerebral hæmorrhage or thrombosis as a result of cardio-vascular disease. The only affliction in which the employment of hyperpnœa requires a considerable amount of care and experience is epilepsy. As voluntary hyperpnœa makes manifest in one way or another lurking abnormalities of the nervous system, it is very apt, when carried to a sufficient degree, to result in an attack of minor or major epilepsy in persons who are subject to such attacks—a procedure which is justifiable only by an urgency of diagnosis.

The action of hyperpnœa upon the nervous system may be compared with that of a drug. The effects of the procedure are, as a matter of fact, brought about by a change in the chemistry of the body fluids. A brief sketch of the nature of this change will, therefore, conduce to a more intelligent understanding of the subject.

II.—The Main Facts about the Blood Chemistry in Tetany.

The literature on the chemical changes in the blood found in connection with tetany is very extensive. For the purpose of the

present study a brief review of the salient features of these changes must suffice.

In a study of parathyreoidectomized animals, MacCallum and Voegtlin [24] found that the administration of calcium salts temporarily relieved the symptoms of tetany, while sodium or potassium salts tended to intensify it. The opinion of these authors, therefore, was that parathyreoprivoid tetany is due to a diminution of the normal calcium content of the blood. As a result of a later investigation along the same lines, MacCallum and Vogel [25] conclude that "the theory that tetany is closely dependent upon a disturbance of the calcium content of the blood is supported by stronger evidence than any other idea."

Howland and Mariott [21] found that during the active symptoms of tetany the calcium of the serum may fall from 10 or 11 to as low as 3·5 mg. per 100 c.c. They call attention to the fact that tetany sometimes occurs from the administration of sodium bicarbonate. They could find no evidence of alkalosis as a factor in the production of infantile tetany. Freudenberg and Györy [14] found that in tetany guanidin is formed in increased quantities and that this poison prevents the utilization of calcium. Cruikshank [10] described, in parathyreoidectomized dogs, a drop in the calcium content of the blood. Immediately after the operation there was a state of alkalosis which, with the development of the symptoms of tetany, passed rapidly into a condition of acidosis.

MacCallum and his associates [26] found that when the pylorus of a dog is occluded and only water introduced, the mucosa of the stomach continues to secrete HCl. The alkali reserve, however, increases and symptoms resembling those of tetany develop. Lemaire and Olivier [23] studied tetany in connection with the chronic vomiting of infancy attributed to pyloric spasm. The administration of bicarbonate of soda aggravated the symptoms, while calcium salts relieved both the vomiting and the muscular spasm. Symptoms of tetany ensuing after the administration of sodium bicarbonate have been reported by Blum [3], Harrop [17], Healy [20], Tileston and Underhill [34], and by a number of other observers.

Ogler [29] takes up in detail the literature of the blood chemistry of tetany in connection with a number of conditions, but passes by the tetany brought about by hyperpnœa with a mere mention. Collip and Backus [9] studied the blood chemistry of tetany brought about by hyperpnœa. Their conclusion is that the symptoms are caused by the production of a mild degree of alkalosis—a reduction of the H-ion concentration of the blood.

Grant and Goldman [16] made a number of experiments on the production of tetany by means of hyperpnœa on two subjects. They studied the blood changes during the development of the symptoms. They found that voluntary movements as well as inhalation of CO_2 prevented the onset of tetany. Among their conclusions is that "forced respiration, by washing out the CO_2 from the alveoli, reduces the CO_2 in the blood, and so tends to make the blood more alkaline than normal."

These citations indicate two points of view. One is that the symptoms of tetany are due to a diminution of the normal calcium content; the other attributes the condition to a state of alkalosis. The two views, however, are not irreconcilable. Wilson and his associates [41], [42], describe a state of alkalosis during the period immediately preceding the attack of tetany in parathyreoidectomized dogs. They found that the injection of acid as well as of calcium salts relieves the muscular spasms. The work of these investigators tends to the conclusion that the action of calcium in such cases may be to cause a relative increase of the acid radicles.

Davies, Haldane, and Kennaway [11], in their experiments on hyperpnœa, observed symptoms of numbness and tingling of the extremities, fibrillary twitchings of the orbicularis palpebrarum and slight Rombergism. These symptoms, which they thought to be due to a state of alkalosis, were in their cases relieved by a few breaths of oxygen. It will be pointed out later, however, that the action of oxygen inhalations, far from relieving the symptoms of tetany, has facilitated their occurrence in a number of cases, and they were never in any case relieved by the administration of this gas.

We are therefore justified in assuming, as the immediate cause of the tetanic state, a diminution of the H-ion concentration in the blood, a state of alkalosis.

Technique.—The subjects, in the recumbent position, breathed in synchrony with one or more sounds of the beating of a metronome. The rate of breathing, made to accommodate the particular capacity of each subject, varied between eleven and fourteen a minute. The breathing was as deep as possible, and a uniform depth of movement was maintained by means of a simple instrument fastened around the subject's chest; this consists of a pair of hands which diverge with the expansion of the thorax, and which approach each other as the circumference of the thorax is narrowed at each expiration. The upper ends of the hands of the instrument are connected with a tape, whose

length is adjusted at the beginning of the experiment, when the subject has taken as deep a breath as possible. The person is then instructed to breathe so deeply that the tape will become stretched at each inspiration.

III.—General Considerations.

Plastic tonus.—It has been shown by Sherrington [33], Brown [5], and others that the rigid muscles of the decerebrate animal are plastic, that is, they are capable of retaining new lengths imposed upon them by passive manipulation or in other ways.

In the present study it appeared at first that the rigid muscles were not possessed of this property to any notable extent. The procedure used in the attempt to elicit this phenomenon was flexing or extending the rigid segments of a limb. With very few exceptions the segments returned to their original positions soon after they were released. Upon investigation the technique, in its application to persons, was found to be faulty. In those cases in which the contraction of the muscles was very strong, passive stretching was too painful a procedure to be carried out with the necessary degree of completeness. Experiment was therefore reduced to cases in which the degree of rigidity was relatively slight and the amount of stretching was, therefore, insufficient to cause pain. A change in the technique was followed by striking results.

At the beginning of the experiment the segments of a limb were fixed in a desired posture by means of bandages. When a degree of rigidity that was deemed sufficient had set in, the bandages were removed. The limb was then found to retain the artificial posture determined by the bandage. All sorts of patterns were produced in this way, and some of these are shown in fig. 2. If after the limb was released hyperpnœa was continued, the segments gradually reverted to the position which they habitually assume under those conditions.

It will be readily seen that this process of "moulding" a limb into a desired pattern is equivalent to that of passive stretching of contracted muscles. In the demonstration of the plasticity of the rigid muscles of the decerebrate animal, the rigidity is first induced and the length of the muscles then determined. In the demonstration of the same property of the tetanic musculature of the living person the length of the muscles was determined first and the degree of their tonicity afterwards.

The special significance of the phenomenon described lies in the fact

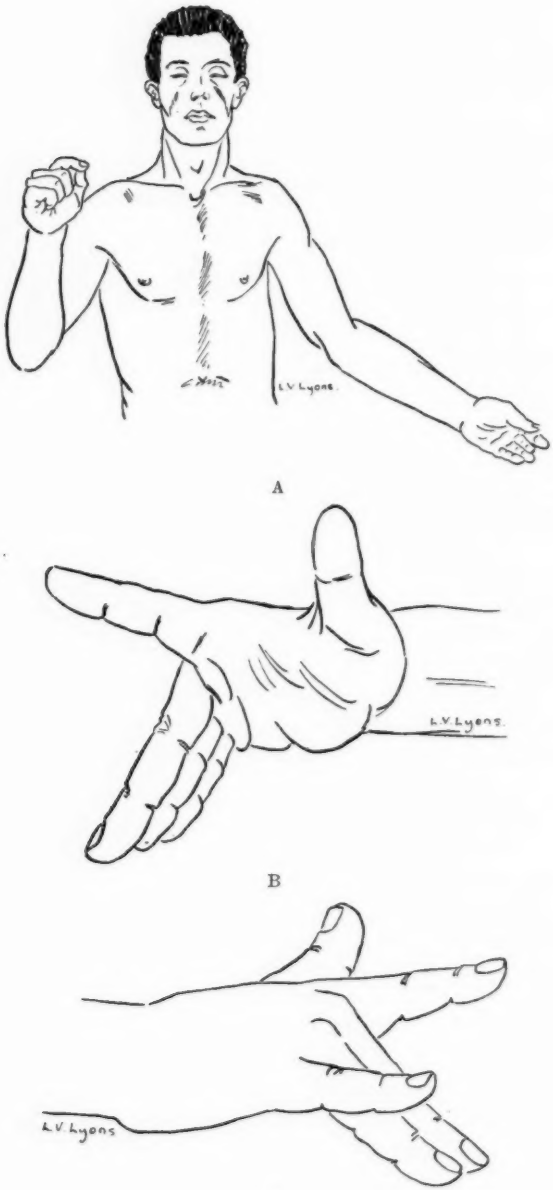


FIG. 2.—Plastic tonus. A, a drawing from a photograph, taken two minutes after the cessation of hyperpnœa, with the patient in the sitting position. Before the beginning of the experiment the left limb had been fastened to the bed-sheets. Compare the posture of the rigid limbs with that of the same subject shown in fig. 3. B, a free-hand sketch. C, from a photograph; the "moulded" right hand of a patient not mentioned in this study. In E, the posture of the thumb and forefinger; in C that of the thumb, forefinger and little finger, have been determined by bandages before the beginning of the experiment. The rest of the fingers had been allowed to go free, and the resulting posture of these free fingers is that which they habitually assume under hyperpnœa.

that since the segments of a limb remain in any position in which they are placed, the antagonistic muscles must contract with equal force.

The reflexes.—In the early stage of tetany the tendon reflexes are increased. Following this is a period when these reflexes are once more of normal briskness and amplitude. With a still further increase in the degree of rigidity, the tendon reflexes are difficult, and finally impossible, to elicit.

The diminution and disappearance of the tendon reflexes when the degree of rigidity has risen above a certain point may be due to a cause which needs further investigation. If the beginning contraction of the muscle whose tendon is struck must necessarily precede the relaxation of its antagonist, the former muscle, if already contracted to its utmost capacity, cannot, by a further contraction, initiate a relaxation of its antagonist; no change in the lengths of the muscles could under such conditions take place, and, therefore, no movement at the joint. Olmsted and Warner [30] found, indeed, that "in the reciprocal action of antagonistic muscles . . . contraction occurs slightly before relaxation."

Since the tendon reflexes are at first increased and then diminished or lost, it will be seen that between these two stages they must pass through one when their appearance is that of the normal jerk.

The abdominal, cremasteric and the plantar reflexes are slightly increased. Special instances in which certain reflexes, both superficial and deep, are perverted, increased, diminished, or lost under the conditions of the experiment, will be referred to later.

The conscious state.—Certain of the sensations become more acute, others are blunted. The appreciation of gross contact appeared to become heightened. The pain produced by the prick of a pointed instrument, or by deep pressure with a blunt one, or by the hyperextension of the joints, was felt more acutely during hyperpnœa. The same was true of the sensations of temperature above and below moderate degrees. The following instance illustrates the state of this order of sensations:—

Case 3.—R. D., an epileptic boy of 13, had been subjected to voluntary hyperpnœa over 150 times, and had become so habituated to it that the procedure caused him hardly any discomfort. One day he exhibited great restlessness and inattention during the experiment and broke out in tears at the end of it. Asked for the reason he explained that a slight cut on his large toe had caused him a great deal of pain during the experiment.

The reactions to tickling or scratching, to grating and dissonant sounds, to uncomfortable postures of the body, to the higher degrees of

temperature and humidity of the air—the so-called affective reactions—have been found more pronounced during hyperpnœa.

With the progress of tetany there occurred in the great majority of cases a profound diminution of the power of attention. Since the faculty of attention is a prerequisite to discriminative sensation, the latter must suffer during the tetanic state of hypernœa.

The subjective sensations are those of dizziness, and of numbness, tingling and stiffness in the limbs affected by the rigidity.

The sensation of dizziness, which occurred in nearly all persons subjected to hyperpnœa, is the first to appear. While the person is in the recumbent position it is usually very slight. It is experienced most when the person rises to his feet before the rigidity has worn off. The subject may then stagger and complain of vertigo.

Since the appreciation of gross contact remains undiminished, the sensation of numbness must be due to an effect upon the sensory area of the cerebral cortex.

The feeling of stiffness in the affected limbs is usually slight. In a few cases, however, it amounted to a sense of pulling of a joint, sufficiently painful to necessitate the placing of the limb in a more favourable position, or to interrupt the experiment.

Special subjective sensations and wide deviations from the normal state of consciousness are dealt with separately.

Volitional movement of the rigid parts.—The power of volitional movement was hampered by the rigidity in a purely mechanical way, but was otherwise entirely independent of it. When the rigidity induced was extreme, so that it was impossible for the experimenter to flex or to extend the part involved, the volitional effort on the part of the subject was ineffective as well. The reverse was likewise true: in every instance in which the rigidity was of a degree which made passive movement possible, the volitional effort of the subject accomplished as much.

Abnormal involuntary movements.—Tremor of the facial musculature was an almost constant phenomenon in the first few of a series of experiments performed upon the same person. With the repetition of the experiment the tremors became less conspicuous and finally disappeared. This was true of other varieties of abnormal movements which appeared during hyperpnœa.

The sign of Chvostek has been frequently encountered in the experiments, that of Trousseau but rarely.

The selective incidence of the rigidity in the better trained musculature.—In right-handed persons the right hand was the first to be

affected by the rigidity, while the left hand was the first to be affected in frankly left-handed persons. A number of left-handed persons, however, are ambidextrous; in such persons the rigidity appeared simultaneously in both hands.

The action of oxygen, of caffein, of the bromides and of phenobarbital.—The action of these drugs on the effect of hyperpnœa has been tested in a number of cases. Biggs [2] has shown that the action of oxygen in muscular exercise is to postpone and to relieve fatigue. Inhalations of oxygen in the present experiments appeared to have no other effect than to facilitate the effort involved on the part of asthenic persons. Hyperpnœa was therefore more active and the onset of tetany was, in consequence, more rapid. The procedure by which the oxygen is introduced was, however, disagreeable to most of the persons experimented upon, and the degree of distraction of the attention caused by its administration operated on the whole as an unnecessary interference.

The action of caffein citrate was uniformly to shorten the time of onset of the manifestations and to make them more pronounced. In this respect the drug operated with equal efficiency in both normal and subnormal persons. The respiratory movements became more active and the neuro-muscular phenomena more prominent.

The action of the bromides was the reverse of that of caffein.

Phenobarbital was administered to a number of the epileptics who were subjected to the experiment. Its action was much more pronounced upon the conscious state of the person than upon the musculature. It prevented the occurrence of unconsciousness, and the power of attention was longer sustained. But the onset of the rigidity was only slightly postponed and its degree only slightly lessened. The only definite action of phenobarbital upon the muscular phenomena was to lessen the extent, or even to prevent entirely the occurrence, of involuntary movements as an effect of hyperpnœa.

The action of pain.—In the course of the study it appeared that persons suffering from pain of any kind succumbed to the effects of hyperpnœa with greater facility than those free from it. The following experiment illustrates the efficiency of pain in promoting the manifestations of tetany in hyperpnœa:—

Case 4.—M. N., a man aged 64, weighing 100 lb., suffered from tabes dorsalis for the last twenty-three years. At the time of the experiment he was bedridden, with profound inco-ordination of the limbs and strongly impaired muscle tendon sensibility. The tendon reflexes were absent. He

had Argyll Robertson pupils, beginning atrophy of the optic nerves and a drooping upper eyelid. He was subjected to voluntary hyperpnœa during a severe crisis of shooting pains in the left lower limb. Although the duration of each paroxysm was, as usual, not quite a second, the intermissions were filled with the ache and soreness which follow in the wake of excruciating pain. After five minutes' deep breathing the upper right limb became completely flexed at the elbow, the biceps being palpably rigid. At this point a shooting pain occurred. The patient screamed and moved about in agony. Hyperpnœa was interrupted and the tetanized arm soon dropped to the table in the natural position. After a while the patient resumed deep breathing. Within five minutes the right upper limb once more passed into tetany which again disappeared on the interruption of hyperpnœa. In this manner deep breathing was resumed six times with the same result.

Another instance of the action of pain under hyperpnœa may be seen in the rapid onset of tetany in the "normal" Case 13.

IV.—General Differences between the Manifestations of Tetany in Normal and Abnormal Persons.

The important factors to be considered in this connection are as follows: (*a*) The length of time during which hyperpnœa must be continued before the appearance of any of the manifestations of tetany —the time of onset. (*b*) The presence or absence of abnormal movements and the kind of movements. (*c*) The selective incidence of the muscular phenomena in special parts—the muscle-pattern. (*d*) The conscious state.

(*a*) *The time of onset.*—Definite muscular spasms, abnormal involuntary movements and disordered states of consciousness made their appearance in some cases within less than two minutes; in others certain manifestations barely appeared after active hyperpnœa was continued for over an hour. These two extremes in the time of onset were found in persons afflicted with certain abnormalities of the central nervous system. About midway between these were presumably normal persons; and shading out towards each end were gradations between the normal and abnormal.

The normal line, however, was found to be broad and ill defined, and encroached upon on both sides by definitely abnormal cases. Unless, therefore, some of the reasons for such a state of affairs be determined, a wrong idea of the importance of the time of onset as a distinguishing characteristic between the normal and the abnormal must be obtained.

The essential cause of the neuro-muscular phenomena is a chemical

change in the body fluids, brought about by an over-ventilation of the lungs. The length of time necessary for the production of the chemical change may depend upon the depth and frequency of the breathing on the one hand and upon the subject's body weight on the other. Although these factors can easily be determined, their importance is largely nullified by a number of conditions. Prominent among these is the wide normal variation of the osmotic properties of the alveolo-capillary membrane resulting from slight changes in the force of the blood-flow, from differences in the viscosity of the blood and from other causes. The muscular activity involved in the respiratory act and in the heart beat, by restoring the CO_2 balance in the blood, must tend to subtract from the progressive state of alkalosis. The magnitude of these and of other factors remaining undetermined, the value of the ratio of the depth and frequency of the respiration to the person's body weight loses largely in significance as a measure of the particular susceptibility of the person to the state of alkalosis.

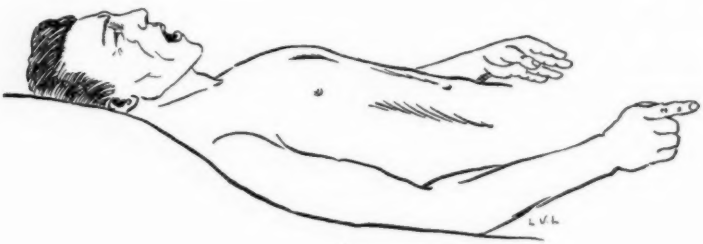
(*b*) *Abnormal involuntary movements.*—From the experiments carried out in connection with the present study it appeared that the nearer a person approached the average normal type, the fewer were the muscular tremors, twitches, athetotic movements, involuntary co-ordinated movements and convulsions. To this rule but one exception has appeared thus far: none of the hemiplegics of the ordinary type experimented upon exhibited involuntary movements to any greater extent than did normal persons. The following is an example of the efficacy of hyperpnœa in bringing about convulsive movements:—

Case 5.—A. F., a woman aged 46, weighing 80 lb. Advanced tabes dorsalis, with a great diminution of pain and tactile sensation throughout the body, a profound impairment of muscle-tendon sense, Argyll Robertson pupils, drooping upper eyelids, partial optic atrophy, muscular wasting, Charcot joints, painless fracture of bones and painless loss of teeth.

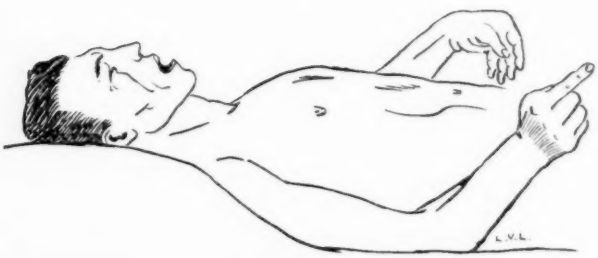
After seven minutes of deep breathing the upper limbs were suddenly thrown into a convulsion. They were raised at the shoulders, semiflexed at the elbows, hyperextended at the wrists and the metacarpo-phalangeal joints and flexed at the interphalangeal joints of the fingers. After a few irregular vibratory movements of large amplitude the limbs remained in the posture described, high in the air in front of the patient. With the cessation of hypernœa the upper limbs became, in the course of about twenty seconds, relaxed. She then resumed deep breathing. Eight minutes later the sole of the left foot was gently scratched. In response both lower limbs were raised in a convulsive movement followed in a few seconds by convulsions of the upper limbs. All four limbs executed rapid vibratory movements of large

range for a few seconds, and then remained rigid high in the air like the limbs of a dog placed on his back. The patient was dazed and hyperpnœa was automatically discontinued.

(*c*) *The selective incidence of the muscular phenomena.*—In normal persons the onset of tetany was signalled by a slight tremor of some of the facial muscles, especially those of the lower eyelids. This was followed by rigidity of the lower portion of one side of the face, generally the right. A little later a sustained spasm appears in one or other hand, depending upon whether the person was right-handed or left-handed. In another minute or so the lower portion of the face and both hands were involved: the lips were pressed close to the teeth, the orifice of the mouth became circular; the hands assumed the well known form of the "obstetrician's hand," that is the thumb and fingers were closely adducted, extended at the interphalangeal joints and semiflexed upon the metacarpus. In a few instances a slight flexion of the hands upon the wrists was observed and in one instance, to be detailed later, there occurred an extreme abduction of the hand. Even when a high degree of rigidity was present in the face and hands, no visible manifestations of tetany could, by inspection or palpation, be discovered in any other portion of the body or limbs.



A



B

FIG. 3.

FIG. 3.—*continued.*

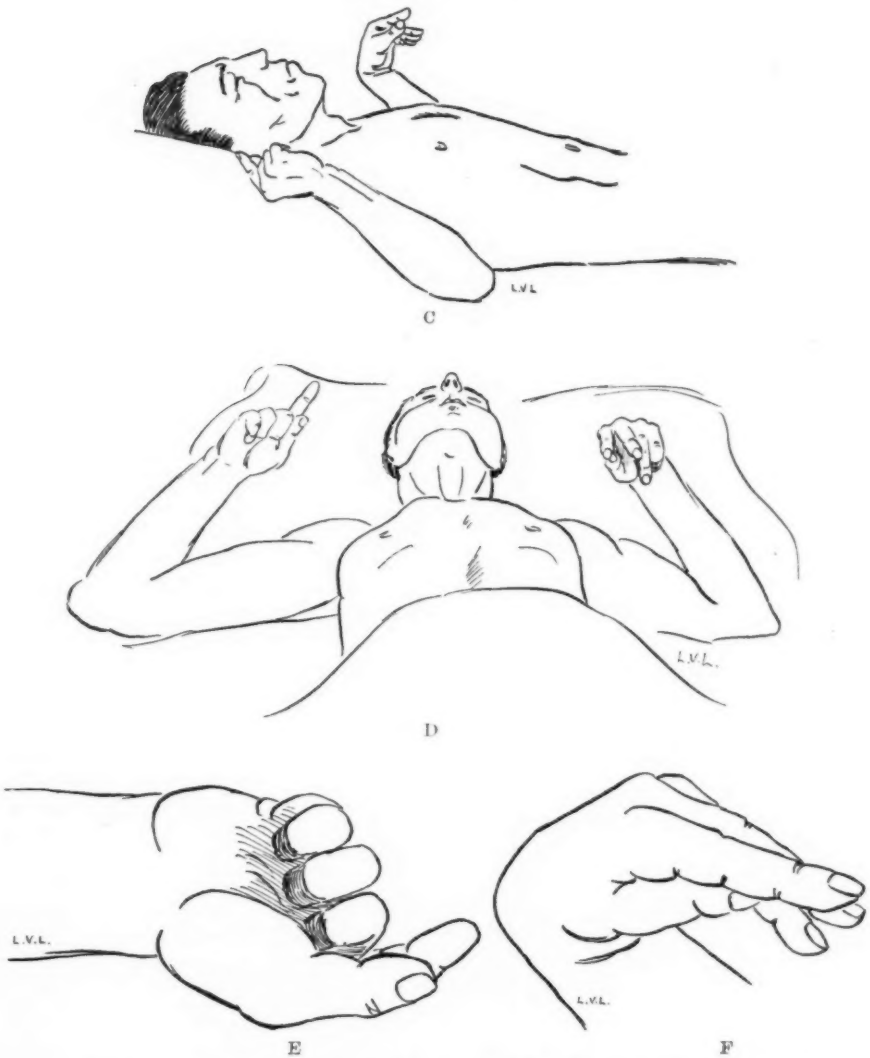


FIG. 3.—Abnormal tetanic postures. Drawings made from photographs. The fingers of the left hand only are in the "normal" posture, the rest of the segments of that limb as well as all the segments of the opposite limb have formed abnormal patterns. A, B, C, D and E, show the postures assumed after 10, 15, 20, 25 and 30 minutes' hyperpnœa respectively. Compare the posture of the limbs with that shown in fig. 2, A.

In persons afflicted with defects of the nervous system the incidence of the rigidity exhibited wide variations from that of the "normal." The following experiments exemplify this:—

Case 6.—S. O., a healthy looking man aged 25, was admitted for observation to the Neurological Wards of Mount Sinai Hospital, in the service of Dr. Sachs. The patient complained of obscure frontal headaches, and of convulsive attacks limited to the right side of the face and the right upper limb, which had recurred on three different occasions within the last year. Thorough medical and neurological examinations revealed nothing abnormal. Not the least difference in the reflexes of the two sides could be discovered, and no convulsive attacks were observed by the attendants.

The writer was granted the privilege of subjecting this patient to the experiment of hyperpnœa. The result indicated a definite deviation from the type of tetany that occurs in normal persons. The striking difference in the muscular pattern on the two sides may be observed in the drawings (fig. 3) made from photographs.[1] Apart from the inequality of the muscular pattern on the two sides, the other deviations from the normal were in this case as follows: Violent tremors of the musculature of the right side of the face, of the right upper limb and of the anterior muscles of the right thigh; strong retraction of the head producing the picture of opisthotonos (fig. 3, D), and of the toes, which became hammer-shaped.

A second experiment on this patient was made one week after the first. In the drawing made from a photograph (fig. 2, A) it is seen that the very abnormal posture of the right hand was exactly the same as on the first occasion. The left upper limb had been bandaged at the beginning of the experiment for the purpose of demonstrating the plasticity of the rigid muscles.

The exact meaning of the anomalies of the induced tetany in this patient remains for the present unknown.

Case 7.—H. B., a man aged 40, with advanced general paresis. Blood and spinal fluid findings positive for syphilis.

His mentality, although very defective, was sufficiently clear to enable him to co-operate in the experiment. After breathing deeply for three minutes the right hand and fingers suddenly leaped into a position of hyperextension at the wrist, hyperextension and abduction of the thumb, semiflexion of the fingers at the metacarpo-phalangeal joints and extension at their distal joints, with the exception of the index finger which was flexed at the proximal phalangeal joint. Fig. 4 is a sketch of the bizarre posture.

Other instances will be observed in this study.

In the consideration of the different selective incidence of the

[1] I wish to thank Dr. L. Visburgh Lyons who executed the beautiful sketches in figs. 2, 3, 4, 6 and 7.

muscular phenomena in normal and abnormal persons, the factor of right-handedness or left-handedness serves to make judgment difficult in certain cases. When the incidence of the rigidity is in the right hand in a right-handed person who is afflicted with disease of the left side of the cerebrum, other factors must be taken into consideration before conclusions can be drawn.

(*d*) *The conscious state.*—The changes in the conscious state which take place in average normal persons have been described in the preceding chapter. Persons afflicted with abnormalities of the central nervous system have been found to exhibit a great diversity of abnormal states of consciousness. Some have complained of sensations of cold, others of a sense of intolerable weight on the limbs affected by the rigidity, others of sensations of swelling, of electric currents, of the loss of sight, of deafness. No disturbances referable to the olfactory or

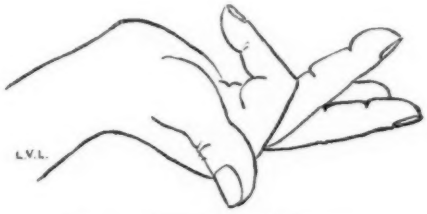


FIG. 4.—Abnormal tetanic posture.

gustatory apparatus have been encountered. Complete loss of the power of attention occurred regularly in a number of the "abnormal" cases. Such an occurrence, of course, automatically determines a return to the normal state. In a few cases, however, instead of diminishing, the frequency and depth of the respiratory movements increased progressively. The following is an example :—

Case 8.—F. S., a man aged 31, has been subject to major attacks of epilepsy for the last nine years. Except for a facial asymmetry and hypospadias, examination revealed nothing abnormal.

He was subjected to voluntary hyperpnœa. As he appeared to be utterly incapable of breathing in rhythm with the metronome after the lapse of a minute or so, he was permitted, during the first four experiments, to breathe at the rate which suited him best. The result was that the respirations increased progressively in rate and depth. Intense rigidity of the right side of the face and of the hands ensued in six minutes. As he appeared utterly insensible to requests to cease breathing deeply, he was raised up and shaken into a rational state. For a number of minutes following he seemed dazed

and would not reply to questions. He then informed me that he was experiencing the same sensations of "flashes and a queer shaking within the eyes" as before an epileptic attack.

During the succeeding experiments this patient was requested to breathe in rhythm with every three beats of the metronome and to strike a percussion hammer which he held in his hand against the table at every third beat. The procedure was successful in maintaining his attention for longer periods of time. The loss of attention was signalled by his failure to strike the hammer. If allowed to continue deep breathing beyond that point, rigidity rapidly set in and the sensation of "shaking within the eyes" appeared. One of the records is reproduced in fig. 5.

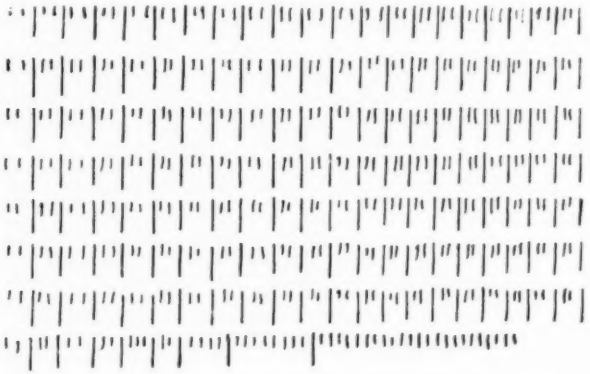


FIG. 5.—A record of the power of sustaining attention under hyperpnœa. The lines were drawn by the experimenter, one for each beat of the metronome. The longer lines were made each time the patient struck the hammer (see text). It will be seen that the end of the record contains no long lines.

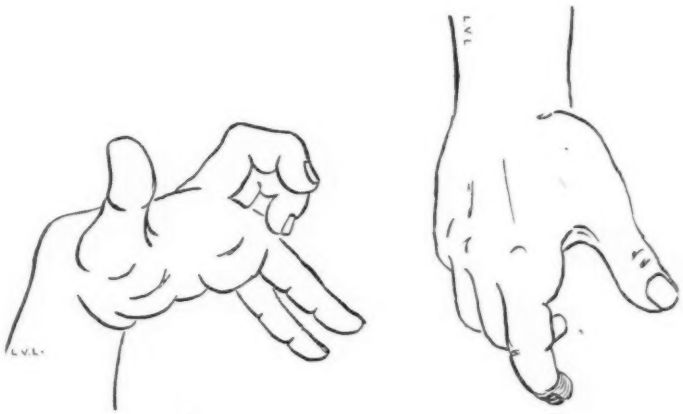
In another class of abnormal persons a general diminution of the conscious state asserted itself by a tendency to fall asleep, or by repeated uncontrollable yawning.

Case 9.—L. C., a young woman aged 22, weighing 124 lb., was an epileptic since childhood. There was defective co-ordination, impaired stereognosis, absent abdominal reflexes and occasionally Babinski's sign on both sides. Her mentality was roughly that of a child of 10 or 12.

After a few minutes' deep breathing she began to yawn and to become somnolent. By dint of urging, however, she continued the exercise. Rigidity appeared in the hands five minutes after the beginning of the experiment. The right hand was supinated, the thumb abducted and the fingers separated and slightly flexed at all joints. The left hand was pronated, the thumb abducted, the fingers were widely separated, the index and middle being hyperextended at the metacarpus and extended at their own joints. The resulting postures are shown in fig. 6.

Ten minutes after the beginning of hyperpnœa it was no longer possible to keep the patient awake. As she fell soundly asleep hyperpnœa was automatically discontinued and she was easily awakened a minute later.

That complete unconsciousness occurs under the conditions of the experiment with relative ease in epileptics was mentioned in the introduction.



A B

FIG. 6.—Abnormal tetanic postures.

V.—TETANY IN NORMAL PERSONS.

The task of elucidating the principles of the nerve-mechanism which gives rise to the numerous and varied manifestations of tetany brought about by hyperpnœa is made difficult by many opportunities for error. Unless a more or less concrete idea be gained of the appearance of the picture of tetany in presumably normal persons, its great complexity in the case of persons affected with different disorders of the nervous system must defy any attempt at analysis. The following cases of "normal" persons are advanced in order to render easier of solution the problems which will subsequently present themselves.

Experiments on Six Normal Persons showing Slight Abnormalities in Five.

The first experiment in the first case is illustrative of possible loopholes of error in the application of the technique.

Case 10.—H. B., a medical student, aged 21, weighing 143 lb.; was right-handed.

With the exception of the mild affections of childhood he has had no special diseases. Physically and mentally he appeared to be in every way normal.

Apparently active hyperpnœa, continued for forty-five minutes, had resulted only in a slight exaggeration of the tendon reflexes and a mild sensation of dizziness. It appeared later that the hyperpnœa, which appeared to be active, was in reality, from motives of fear of ill consequences, instinctively feigned. By a retraction of the abdomen, an expansion of the chest occurred without a corresponding expansion of the lungs.

A second experiment was performed on this young man after the administration of caffein with the following results :—

Five minutes : A slight tremor of the right lower eyelid. Beginning rigidity of both hands, which is more conspicuous in the right.

Eighteen minutes : The lower portion of the face is contracted so that the lips approach the form of a circle pressed close to the teeth. The rigidity of the hands is very strong. The form is that of the normal tetanic "obstetrician's hand."

After hyperpnœa was discontinued he could not speak for about a minute on account of the rigidity of the musculature of the lower part of the face. All rigidity disappeared in two minutes. His subjective sensations were those of stiffness in the muscles of the face, neck and upper extremities, of tingling and numbness in the fingers and along the ulnar borders of the forearms, and of slight dizziness.

A third experiment was performed after the administration of 60 gr. of bromide in broken doses. Active hyperpnœa continued for thirty minutes resulted in a barely perceptible adduction of the right thumb. There were no other symptoms of tetany either objective or subjective.

Case 11.—F. M. L., a medical student aged 24, weighing 143 lb. ; was right-handed.

In addition to the milder afflictions of childhood he had had the following diseases : at the age of 3, acute rheumatoid arthritis ; at the age of 10, typhoid fever ; two years later, a gangrenous appendicitis with peritonitis for which he was operated on. The following year he was operated on for right inguinal hernia ; a year later he had a severe attack of rheumatoid arthritis involving all the joints of the extremities and the neck ; the same year his hypertrophied and infected tonsils were removed.

Notwithstanding all these diseases he appeared to be at the time of the experiment in excellent physical condition, except that he was rather out of training. The deep and superficial reflexes were active and equal on both sides, and there were no other neurological abnormalities. The right lower quadrant of the abdomen was marked by two scars, the result of the two operations he had undergone.

Voluntary hyperpnœa resulted in the following :—

Three minutes : All the tendon reflexes are increased.

Ten minutes : A fine rapid tremor of the right upper eyelid. Beginning

normal tetany in the right hand. The tendon reflexes are no longer exaggerated and the right arm-biceps has become inconspicuous and difficult to elicit.

Thirteen minutes: A strong tremor of the entire facial musculature of the right side. The left hand is involved in normal tetany in addition to the right.

Fifteen minutes: Both upper eyelids are now affected by the tremor. The tetanic spasm is very pronounced in both hands. The left patellar reflex is very much greater than the right.

Twenty minutes: The abdominal reflexes are absent on the left side and present on the right (the side operated on).

Twenty-five minutes: In addition to the other phenomena, athetotic movements of all the fingers of both hands. The right biceps-jerk cannot be obtained.

Hyperpnœa was discontinued. At this time the right side of the face was so much contracted that the right eye was nearly closed, and he could not open his mouth to speak. Three minutes later the rigidity disappeared, the deep and superficial reflexes were again normal and equal on both sides. His subjective sensations were the same as in Case 10.

The manifestations of tetany in this young man were exactly the same in a second experiment made for the purpose of testing the effect of caffein citrate. The time for their production, however, was only fifteen minutes. After taking 60 gr. of the bromides, all the phenomena exhibited on the two previous occasions were of a milder degree and the time for their appearance was prolonged to thirty-eight minutes.

The two medical students were from both physical and mental standpoints very similar to all appearances. They were of the same height—5 ft. 10½ in.—and nearly of the same weight. The difference in their ages was not quite three years. They both appeared normal and healthy. Apart, therefore, from any possible hereditary factors which remain unknown, the only reason for the striking differences in the manifestations of tetany in the young men appears to be the fact that the second had undergone a number of severe illnesses. That these illnesses must have resulted in certain permanent injuries of the central nervous system, which became manifested in the effects of hyperpnœa, will appear more clearly when the nervous mechanism which is responsible for the tetanic phenomena is partly discovered in the course of this study.

Case 12.—A. D., aged 36, weighing 165 lb., right-handed, is an artist—a painter—by profession, a man of a high degree of culture and education.

In childhood he had what was most probably tuberculosis of the hip-joint, with the result that the left lower limb is now shorter than its fellow by about 4 cm. and is the thinner of the two. Otherwise Mr. D. is in excellent health, being robust and muscular. His reflexes, including those of the lower limbs, are equally active on both sides.

Subjected to voluntary hyperpnœa, normal tetany appeared in the right hand

in fifteen minutes and became very pronounced in another five minutes. Five minutes later the first signs of rigidity appeared in the left hand, and at the same time the right side of the lower part of the face became drawn. At the end of twenty-five minutes the mouth was of the normal tetanic circular form, and the rigidity in both hands was intense. The lower left limb was actively extended and rigid. He complained of a sense of stiffness in the lateral abdominal walls, particularly on the left side.

The sensations he experienced were a flush of moist warmth over his body, slight dizziness, a feeling in the limbs which he described as a low buzz of fine tremor, and stiffness of the musculature which appeared to have gone beyond his control.

The spread of the rigidity to a lower limb and to the lateral abdominal musculature is not a "normal" phenomenon. To that extent the otherwise normal Mr. D. is abnormal. It should be noted that Mr. D. lives in the mountains and is a good walker and climber. Since the effort involved in the act of walking is the same in both lower limbs, his shorter and thinner left limb must be the better trained of the two if it is able to keep up with its fellow; it is, in other words, to a greater extent under the control of the cerebrum. The lateral abdominal musculature, especially that on the lame side, is, in such cases, called into action to a greater extent than it is in persons whose lower limbs are equally strong. With these facts in mind, the reason for the rigidity of the abnormal left lower limb and the abdominal musculature in this case will become clear in the course of this study.

Case 13.—I. D., a woman aged 38, weighing about 135 lb., a sculptress, was frankly left-handed.

For the last few years she has suffered almost continually from dull pains at the back of the neck and shoulders. Otherwise she has been in good health all her life.

Five minutes of voluntary hyperpnœa resulted in the onset of tetany in the left hand. At this point she complained of intense dizziness and the experiment could not be carried further.

Case 14.—D. E., a boy aged 11, weighing 72 lb., is right-handed, but his mother states that as an infant he grasped things with his left hand. His mother is left-handed, his father is right-handed.

The boy is well-nourished and healthy, but neither wiry nor robust. Although he is very intelligent and reads with avidity and learns quickly, he lacks the faculty of translating his knowledge into tangible forms. Thus he has no patience in finishing an essay begun, or in the completion of a manual task. In the words of his mother, he is wanting in the faculty of "creativeness."

After the first few minutes of voluntary hyperpnœa, the boy began to exhibit a loss of attention both to the beating of the metronome and to the

movements of the expansometer. He had to be urged or reminded continually of the task before him. The reminders, effective at first, soon became futile. He continued the exercise, however, though in an utterly disorganized manner.

Ten minutes after the beginning of hyperpnœa the boy had a sensation of numbness in the face and hands which was, according to him, equal on both sides. Within fifteen minutes a slight degree of normal tetany appeared simultaneously in both hands.

Case 15.—A. D., a boy aged 12, weighing 75 lb., wiry, robust, and very intelligent. He was left-handed as a young child. At present he writes with his right hand only, but is ambidextrous in other manual actions. He was subjected to voluntary hyperpnœa with the following results :—

Seven minutes.—Athetotic movements of the right fingers.

Eight minutes.—A sensation of numbness in the left hand.

FIG. 7.—An abnormal tetantic posture in a normal child.

Ten minutes.—Beginning tetany in both hands, which is perhaps slightly more pronounced in the left. The upper limbs are actively extended at the elbow, the hands are strongly and to the utmost extent abducted (bent in the direction of the thumb) at the wrists, the three outer fingers are completely and strongly flexed at all joints, while the index finger, which is fully as rigid as its fellows, is only semiflexed at all joints, thus standing out high above the others ; the thumb is abducted and extended at all joints. The posture is exactly the same in both hands (fig. 7).

Thirteen minutes.—The rigidity of the hands has become more intense. The posture remains the same, except that the thumbs are now slightly adducted. The sensation of numbness is felt equally in both hands.

It will be seen that of the six cases given, only one, the first, appears to be lacking in any abnormality ; the rest are in some slight respects abnormal. To ordinary appearances, however, all the six are normal, and may be taken to represent the average normal type of person.

VI.—Tetany in Persons with Disease of the Central Nervous System.

Experiments in Cases of Transverse Lesion of the Spinal Cord, in Hemiplegia and Quadriplegia.

Case 16.—I. G., a man, aged 30, weighing 110 lb., sustained an accidental fracture of 11th thoracic vertebra seven years ago, followed by operation on the spine.

At the time of this study the musculature of the thighs is moderately spastic. The parts below the knee are markedly wasted, the anterior tibial muscles being flaccid, the posterior rigid. The feet, which are cyanotic, swollen and glossy, are dropped so that the man walks on his toes. The patellar reflexes are absent; that of the Achilles tendons is inconspicuous and difficult to elicit. There is analgesia over the areas of distribution of the fifth lumbar and the fourth and fifth sacral roots, a diminution of the sense of vibration over the entire area of distribution of the lumbo-sacral cord and a saddle-shaped area of anæsthesia over the inner gluteal regions. Otherwise the patient is in good physical condition.

Voluntary hyperpnœa continued for twenty minutes produced the following results: From the beginning to the end of the test there was a marked and progressive sustained contraction of the entire skeletal musculature (with the exception of the anterior tibial group) which was most conspicuous in the lower limbs. Both upper limbs became flexed to the utmost degree at the elbows, wrists and all the finger-joints, with the thumb pressed into the palm of the hand. The arms were pressed to the sides of the body. The lower limbs were very strongly extended, and adducted with such vigour that it was impossible to separate them. The musculature of the calf became prominent and hard to the touch. The anterior tibial muscles remained flaccid. There was a line of profuse sweating along the edges of the feet. The only subjective sensation was one of numbness in the hands.

Case 17.—L. R., a right-handed man, aged 55, weighing 150 lb., had a tumour of the spinal cord at the level of the third cervical vertebra. The symptoms began six years ago. A laminectomy of the fourth, fifth and sixth cervical vertebræ five years ago showed the cord to be softened and swollen.

At present the patient's condition is as follows: A considerable degree of atrophy of the extensors of the forearms and the small muscles of the hands, with fibrillary twitchings. The musculature of the lower limbs is thin and spastic. The patellar reflexes are exaggerated. The right abdominal reflexes are absent and Babinski's sign is present in both feet. From the level of the third cervical segment down, sensation is defective, the distribution of the defects being in irregular patches. High up around the neck is a belt of hyperæsthesia.

The effects of hyperpnœa, continued for twenty-five minutes, were as follows: A few minutes after the beginning of the experiment the fibrillary twitchings of the musculature affected by the atrophy became more pronounced.

This was followed a little later by a strong tremor of the anterior muscles of the thighs, the tremor becoming finer with the onset of rigidity in those limbs. Babinski's sign then became strongly accentuated in the right foot, and the patellar reflexes on both sides were accompanied by a transient clonus. Towards the end of the experiment the thighs were adducted with great force. There was no sign of rigidity in the upper limbs.

The motor disabilities in the last two cases are due to the flaccidity of some muscles and the hypertonicity of others. Upon the flaccid musculature in the two cases hyperpnœa had no effect, except to accentuate the fibrillary twitchings in Case 17.

From clinical and pathological experience it is assumed that the hypertonicity of certain muscles in these cases is due to injury of the cortico-spinal tract. The prominent features of the effects of hyperpnœa was the extreme degree of rigidity of the muscles which had been partially deprived of the influences carried by the pyramidal system. The phenomenon is all the more striking when the distribution of the rigidity under the conditions of the experiment in normal persons is considered. Even after long continued deep breathing, when the rigidity of the face and hands becomes intense, the musculature of the lower limbs is but slightly affected in normal persons. A hypertonicity of the musculature of the lower limbs was always inferred from the slight increase in the tendon reflexes, though it could not be recognized by inspection or palpation. Since the left lower limb of the normal person, A.D. (Case 12), was abnormal, the rigidity which ensued in that limb does not argue against the general rule. Little doubt, therefore, remains of a special predilection of the rigidity brought about by hyperpnœa for the musculature deprived of the impulses carried by the cortico-spinal system. Whatever doubt there may be will be dispelled by the observation of the effects of hyperpnœa in cases of injury to that system located above the spinal cord. There are reasons for believing, however, that injury to the cortico-spinal system is only partly responsible for this excess of rigidity, and that it must be partly attributed to other nervous mechanisms.

In Case 16 the degree and extent of the rigidity of the upper limbs was above that which is seen in normal persons. In that patient, it will be remembered, the portion of the cortico-spinal tract in relation with the motor neurons of the upper limbs was intact. The man's feet, however, were defective, and he walked on his toes. In addition to the ordinary functions of the upper limbs he was therefore compelled to develop in them a new function—a means of support in the act of

walking. Such development of a new function is the office of the cerebral cortex. The patient's upper limbs were, therefore, to a greater extent under the control of the cerebrum than is ordinarily the case, and the higher rank of the nervous structures involved facilitated the overthrow of their balance. This instance is, therefore, paralleled by the normal Case 12, in which the greater domination of the left lower limb by the cerebrum resulted in its rigidity under the conditions of the experiment. The principle involved in both cases is the same as that which determines the greater susceptibility of the right hand in right-handed persons and of the left hand in left-handed persons.

A notable feature of the experiments in Cases 16 and 17 is the fact that the impairment of the sensations, including that of muscle-tendon sense, had no influence upon the degree of rigidity produced by hyperpnœa. These two cases, however, do not furnish sufficient data for an intelligent consideration of this phenomenon. Its discussion will therefore be taken up in a succeeding section.

From the results of experiments in cases of cord injuries the assumption was made that the seat of predilection of the rigidity produced by hyperpnœa was in muscles which had been deprived of the impulses carried by the cortico-spinal tract. The truth of this assumption was tested by subjecting to the same experiment persons affected with injury of that tract at a level above the spinal cord.

A number of patients with hemiplegia were subjected to the test. The symptoms presented by these patients were of the classical kind: a slight degree of spasticity, semiflexion of the upper and extension of the lower affected limb, the loss of the abdominal reflexes, exaggeration of the tendon reflexes, and the signs of Babinski and of Hoffman on the affected side. Their ages ranged between 39 and 68. They were all sufficiently recovered to be up and about.

Notwithstanding the fact that these patients experienced difficulty in carrying out deep breathing, tetanic manifestations ensued in from five to fifteen minutes on the affected side. No apparent change took place on the sound side within that length of time.

In a case of residual quadriplegia (due to syphilitic disease in the region of the pyramidal decussation) of eight years' duration (J. L., Montefiore), the test was productive, on the whole, of the same phenomena as in the cases of hemiplegia, except that the symptoms of tetany were present on both sides. In this case the rigidity which ensued was particularly intense. The spasm of the adductors of the thighs was so violent that it was impossible for the examiner to

separate the crossed lower limbs. Mere light touching of the soles of the feet produced a violent trembling which involved in succession the toes, the foot, and the entire leg. The emotional reactions were in this patient remarkably pronounced. The least touch of the abdomen resulted in an attack of uncontrollable laughter, and somewhat later in the course of the test outbursts of violent laughter ensued in response to any remark made by the examiner.

All the hemiplegics examined in connection with the present study were right-handed persons, and were paralysed on the right side of the body. Since the effects of hyperpnœa are more pronounced on the right side in right-handed persons, the increase of the manifestations of the spastic paresis in these patients loses in conclusiveness to a certain extent. But in the case of quadriplegia, in which both pyramidal tracts were injured, the effects of hyperpnœa were manifested almost equally on both sides of the body. Moreover, the hemiplegics breathed very poorly. Yet the onset of tetany in all these cases was unusually rapid. The factor of right-handedness must, therefore, have played in these cases a subsidiary part only.

It is seen, then, that the incidence of the rigidity in these patients, as well as in the patients with injury of the cord, was greater in the muscles which had been partly freed from the influence of the cortico-spinal system. The conclusion, however, that this increase of rigidity was due solely to a further incapacity of the cortico-spinal system is not justified, for in no case of profound injury of the cortico-spinal tract is the muscular rigidity so great as that which ensued repeatedly in my experiments. Nor can the extreme degree of rigidity experimentally produced have been due to a *complete* suspension of the function of the cortico-spinal system; for, in injury to the cortico-spinal system in man, volitional effort is not only ineffective in bringing about muscular contraction, but it is not referred by the subject to the muscles. One such patient, indeed, informed the author that his volitional effort to move the paralysed limb was entirely "in the head." The incapacity in such cases is due not so much to the muscular spasticity as to the inability of the volitional effort to reach the muscles.

Such is not the case in other forms of muscular rigidity. Walshe [35] recently emphasized the fact that the only obstacle to movement in the rigidity of extrapyramidal disease is the mechanical obstacle of the rigidity itself. It is, indeed, a familiar fact that no matter how great the rigidity in such cases, the patient is always able to overcome it to a certain extent by the exertion of a volitional effort. When such a

patient is requested to localize the volitional effort, he refers it to the muscles.

In the case of the rigidities experimentally induced in persons with residual defects of the cortico-spinal system, volitional effort was productive of the same result as in the class of cases mentioned in the preceding paragraph. When the rigidity induced was extreme no movement could be produced in response to volition, but the person referred the effort as having its seat in the muscles. When the rigidity, on the other hand, was not extreme, the subject was able, by the exertion of his will, to move the rigid segment of the limb against the mechanical obstacle of the contracted antagonistic muscles.

Since effective power of volition was preserved, the function of the pyramidal tract could not have been totally suspended during the experiment.

The great excess of rigidity in the muscles partially deprived of cortico-spinal impulses must, therefore, in large part be due to the action of hyperpnœa upon another neuron system as well.

The observations of Gowers [15], Brauer [4], Collier [8], Walshe [36], Riddoch [31], Dowman [12], and of a number of others who have studied recent cases of transverse injury to the spinal cord, point unmistakably to the conclusion that the human spinal cord is endowed with a certain amount of independence of function. Riddoch's observations are of special interest as showing that the caudal portion of the severed cord is possessed of those elements essential for the production and distribution of tonus which make movement possible: "In all patients" with complete division of the cord, observes that author, "when reflex contractions occur in one physiological group of muscles, simultaneous inhibition of their antagonists can be demonstrated."

Whatever mechanisms for the production and distribution of muscle tonus reside in the spinal cord, these mechanisms, as shown by the work of the authors mentioned, are very imperfect and undependable. Reflex actions which may be discovered in some persons after division of the cord are not found in others. The movements themselves lack strength and are ill-measured and ill-timed. The tonic mechanism of the human spinal cord, indeed, appears to be subsidiary to the powerful and perfect machinery for the production, inhibition and release of muscle tonus which resides in the brain-stem and the brain.

The fact that in mammals the distribution of muscle tonus to the motor mechanism of the spinal cord is derived largely from the brain-stem—the nucleus ruber (5), (6), and perhaps other cell groups below

the midbrain (1)—is significant of a relationship between the cortico-spinal and the pallio-pontine pathways. The pallio-pontine tract is the first part of the cerebro-ponto-cerebello-rubral pathway. Weed [40] has shown that stimulation of a certain part of that pathway results in an abatement of decerebrate rigidity. Clinical and pathological evidence (43) is likewise in favour of the conclusion that the pathway in question is inhibitory motor in nature. Even Walshe, who rejects both Weed's and Wilson's conclusions [37], agrees with the main point in question [38]—that "there are . . . indications that lesions of the fronto-pontine fibres may play a part in the genesis of spasticity." The recently published experiments of Warner and Olmsted [39] tend to the same conclusions.

In a discussion of the pyramidal system von Monakow [27] calls attention to the fact that destruction of a large part of the frontal cortex, including the precentral convolution in man, does not abolish all motor activities. One of his conclusions is that the cerebellar mechanism is largely capable of compensating for the pyramidal defect. The participation of the cerebrum in the cerebellar mechanism, however, is by means of the pallio-pontine system.

Ogden and Franz [28] have shown that intensive training is capable of overcoming the incapacity resulting from experimentally produced hemiplegia in monkeys to a remarkable degree. Franz, Sheets and Wilson [13] found an astonishing degree of improvement in old residual hemiplegia in man as a result of systematic training. The work of a number of other investigators tends indeed to prove that both in man and in animals a pyramidal defect is capable of being compensated by the development of function of other nerve mechanisms.

The experiments of Lashley [22] throw a great deal of light upon the motor pathway which is thus capable of taking the place of the pyramidal tract. The author has shown that after destruction of any part of the cortex of the rat, acquired visuo-motor habits are retained, provided the area striata remains intact. This means in his opinion that "the conditioned-reflex arcs which mediate the habit must pass to and from the cortex by way of the occipito-thalamic fibres." He overlooked the fact that besides the thalamic fibres the area striata of the cortex gives rise to a contingent of the cerebro-cerebellar motor system —the pallio-pontine. Since the fibres of the pallio-pontine pathway come from nearly every portion of the cerebral cortex, it is no wonder that after destruction of a very large portion of the cortex a certain amount of cerebral motor activity would still be retained.

The functions of the two systems, the pyramidal and the pallio-pontine, are, therefore, similar. The action of the one is upon the motor mechanism of the spinal cord; that of the other upon the red nucleus of the midbrain by way of the cerebellum. It will be readily seen that, under normal conditions, for the production of timed and measured muscular contractions in movement and posture, the activities of both these systems must be perfectly co-ordinated.

The bulk, if not the entire pyramidal system, arises from the precentral convolution. The same convolution, however, gives rise to a portion of the pallio-pontine system. And every portion of the cerebral cortex which contributes to the pallio-pontine system is connected with the precentral convolution by association fibres of different lengths. When, therefore, in addition to a pyramidal defect, the function of the inhibitory motor system with which it is closely associated is depressed as well, what must happen? In addition to the unhampered release of tonus from the motor mechanisms of the spinal cord, there must then also occur an unhampered release of tonus from the mechanism of the midbrain. The result must be a great accentuation of spasticity. Hence the incidence of the intense rigidity during hyperpnœa in those muscles which have been deprived of the influence of the pyramidal system.

VII.—The Action of Pain in accentuating the Tetanic Manifestations.

That the mere appreciation of pain is a function of the thalamus rather than of the cerebral cortex is at present a fact with which neurologists are familiar. As a matter of fact the result of cortical activity is to subdue the sense of pain as well as the muscular reactions to which pain gives rise. "Pain," says Head [19], "is the oldest defensive reaction, and potentially painful stimuli are the basis of all primitive reflexes. It is therefore of importance for higher development that these impulses should be rendered less effective in favour of those impressions which lead to a more general and discriminative response." Certain lesions of the thalamus which sever it from the influence of the cerebral cortex result in that added colouring of the primary sensations which is known as hyper-affect. The discomfort which is ordinarily experienced from painful stimuli of a mild degree becomes under those conditions much more pronounced.

In the chapter on General Considerations attention was called to the fact that painful stimuli, as well as those which give rise to a sense of

general discomfort, are felt more strongly under hyperpnœa than under normal conditions. The instance of a boy (Case 3) who reacted excessively to a slight cut on the toe was advanced as an illustration. The reason for this will now be readily understood. Hyperpnœa has a disabling effect upon the highest cerebral structures. A reduction in the functioning of these structures is equivalent to a lesion of the thalamus which severs that organ from its connections with the cortex. An added colouring of the primary sensations is the result.

In the same chapter the statement was made that the action of pain is to accelerate the onset and to accentuate the symptoms of tetany. The experiments on the normal person, I.D. (Case 13), and on the tabetic patient (Case 4), exemplify this action of pain.

The potency of pain in evoking muscular activity is a fact too familiar to stand in need of much elaboration. The person who submits to an operation without an anæsthetic, clenches his fists, grinds his teeth, strains his muscles. The restlessness of persons afflicted with chronic ache is familiar to all.

One effect of pain is a narrow focusing of attention—a contraction of the scope of consciousness. The latter we have seen in a previous publication [32] to coincide with a reduction or a suspension of the function of the cerebral inhibitory motor apparatus with the release of muscle tonus as a result.

Hyperpnœa and pain, therefore, constitute a highly favourable combination of conditions for muscular activity. Both have a depressing effect upon those highest nerve structures of the cerebrum whose function it is to keep the tonic activity of certain centres in the brain-stem and spinal cord in abeyance.

In the two cases of spinal cord lesions (Cases 16 and 17), as well as in Cases 4 and 5 of tabes dorsalis, we have had occasion to observe under the conditions of hyperpnœa pronounced muscular activity in parts that were more or less anæsthetic. Whether the impairment of the primary sensations has in these cases served to accentuate the degree of the muscular manifestations, remains, for want of proof, unknown. The pronounced degree of the muscular manifestations in these cases, however, points with certainty to the fact that, to say the least, the sensory defect has had no moderating influence upon the degree of muscular activity.

The last statement may appear incongruous with the fact that the presence of pain is productive of muscular activity under all conditions, and that under hyperpnœa its effect is to accentuate the muscular

manifestations. Upon closer examination, however, the seeming incongruity will disappear.

Since the sensory function of the cerebral cortex consists in the *integration* of the elementary sensations, it goes without saying that the absence of the elementary sensations deprives the cortex of its sensory function. The impairment of cortical function results under hyperpnœa in muscular rigidity. A number of other facts exist to prove that a diminution of the sensory function of the cerebral cortex results in muscular activity. The tonic and clonic muscular spasms following unconsciousness in epilepsy, the muscular activity in the first stages of ether narcosis and of alcoholic intoxication, the process of falling asleep and of awakening, are among such facts.

In the same manner that the functioning of a central telegraph station depends upon the numerous calls which arrive along the afferent wires, so does the functioning of the cerebrum depend upon the impulses received from a number of different sensory organs. It is frequently the case, however, that a central telegraph station must, for the benefit of a community, give preference to a certain call; a large portion of the total functioning of the entire system is in such cases for a time suspended, while the particular call is going through. The same is true of certain nerve impulses which arrive to the cerebrum. For the benefit of the entire organism a single nerve-impulse becomes under certain circumstances dominant, and during the time that it remains dominant no other impulses are received. Thus a person who suffers a strong pain is largely insensitive to sights and sounds, to contact, and to other modes of impression. The vast machinery of such a person's cerebrum is largely silent. That the suspension of cortical function results in a release of muscle tonus we have already seen.

This enables us to understand upon a broader basis the reason why on the one hand the partial anæsthesia in Cases 4, 5, 16 and 17 interfered in no way with the muscular activity resulting from hyperpnœa, while on the other hand the presence of pain has the positive effect of favouring muscular contraction.

VIII.—The Part played by the Striate System in the Production of the Muscular Phenomena.

Although the literature on the subject reveals our ignorance of the structure and function of the corpus striatum, nevertheless an impartial review of the evidence afforded by the large number of investigations

points clearly to two facts: (1) that the corpus striatum is interposed as a link in a long and complicated chain of neurons making extensive connections between afferent and efferent cerebral neuron systems; (2) that disease of the corpus striatum, whatever other structures may be implicated, is responsible for an abnormal release of muscle tonus, thus giving rise to disturbances of normal rest and of normal movement.

That the different forms of abnormal involuntary movements—of chorea, athetosis, paralysis agitans, and dystonia—emanate from disorders of closely related parts of a single system may to a certain extent be gathered from the experiments to be presently described.

Experiments in Cases of Athetosis, Choreo-athetosis and Dystonia.

Case 18.—I. C., a girl, aged 11, has never been able to sit, stand or speak. At the age of 2 she had been subject for some time to epileptiform convulsions. With the cessation of these, abnormal involuntary movements of the toes, fingers and the larger segments of the limbs set in and continued to the present time. The movements are of the classical choreo-athetotic type.

She co-operated willingly in the test. From the very beginning until the end of the experiment the abnormal involuntary movements increased in amplitude and extent. In a few minutes every movable portion of the body and limbs was in motion in every direction, including torsion, until the picture became indistinguishable from a typical one of dystonia musculorum deformans.

Case 19.—R. E., a girl, aged 20, suffered in 1919 a prolonged illness which was later diagnosed as lethargic encephalitis. In 1920 she became afflicted with twitching movements of the feet and, later, of the hands and neck. At present the involuntary movements are, during waking hours, almost constant in the fingers. Every three or four seconds there is also a forward movement of the right shoulder and a slight turning of the head to the left.

The result of hyperpnœa was to involve in the abnormal movements every movable segment of the body and of the limbs until the picture became one of dystonia.

Case 20.—G. H., a man aged 25, weighing 100 lb., was never able to walk. At the age of 8 he had epileptiform convulsions for a period of about six months. Abnormal involuntary movements of the athetotic type developed in childhood and continued to the present day.

At present his lower limbs are held semiflexed, and the distal portions of all the four limbs execute irregular movements, which are involuntary and continuous. Upon attempts at speaking the facial musculature and the tongue become involved in irregular movements.

After ten minutes of deep breathing, or rather gasping, the athetotic movements spread to the central segments. They occurred in every direction, including torsion, and were of progressively increasing amplitude. The hyper-

extension of the fingers and wrists in the movements of extension resulted in the momentary assumption of most bizarre postures of the hands. The picture became indistinguishable from one of extreme dystonia.

Since the action of hyperpnœa was to convert the movements of athetosis and of choreo-athetosis into those of dystonia, it became of interest to ascertain the effect of hyperpnœa on patients afflicted with dystonia. The dystonic patients of the Montefiore Hospital were, therefore, subjected to the test. The result was so great an exaggeration of the abnormal movements that the patients were prevented with difficulty from falling off the examining table.

The Quantitative Equivalence of Muscle Tonus in Joint Fixation (Rigidity) and in Movement.

In the foregoing cases of athetosis, chorea and dystonia the result of hyperpnœa was clearly single—a progressive increase of a previously existent movement both with respect to the number of segments involved and to the amplitude of oscillation of each moving segment. Whatever be the nerve mechanism which, in the normal state, holds such movement in abeyance, it is plain that the action of hyperpnœa is to bring about a progressive depression of its function.

We have seen, however, that the action of hyperpnœa in depressing the inhibitory pallio-pontine and cortico-spinal neuron systems was to immobilize the joints by the equal contraction of antagonistic muscles. That these were contracted with equal strength is proven by the experiments on plastic tonus described in the chapter on General Considerations.

It goes without saying that the two inhibitory systems just mentioned must be depressed by hyperpnœa in athetosis, chorea and dystonia, irrespective of any additional structures involved. The question may, therefore, be very well asked: Why did not sustained rigidity of the limbs ensue under hyperpnœa in these cases?

The answer is so simple that if it were not for a singular misapprehension on the part of a number of authors respecting the relation in which posture stands to movement, the question itself need hardly have been asked. It is that the same amount of tonus determined to the musculature of a limb may cause either the movement of the segments of that limb or a state of rigidity. In the first instance there is a difference between the quantities of tonus distributed in antagonistic muscles at any given moment. When the quantity of tonus is greater

in the flexors than in the extensors, a movement of flexion occurs. If now there takes place a redistribution of the total quantity of tonus in the musculature of that limb, so that the difference becomes in favour of the extensors, a movement takes place in the opposite direction—in that of extension. In the second instance the total quantity of tonus in the limb is distributed equally between antagonistic groups of muscles. The result is the fixation of the joints—a posture.

It will be seen, therefore, that the occurrence of a release of muscle tonus is not only not incompatible with the increase of the movements which, under hyperpnœa, takes place in athetosis, chorea and dystonia, but is indeed a necessary condition to such an increase. If the degree of tonicity of a muscle is measurable by the amount of force which it is able to exert by its pull upon the bony levers, then the increase in the quantity of tonus which was determined under hyperpnœa to the musculature of the moving limbs in athetosis and dystonia was very obvious in these experiments. The amount of force exerted in the attempts of the investigator and the assistants to restrain the movements of these patients so as to keep them from falling off the examining table during the experiment was very considerable.

IX.—The Influence of Attention on the Effects of Hyperpnœa. The Influence of the Emotions.

The beginning of the act of deep breathing in synchrony with the sound of the metronome and the movements of the expansometer is marked in all persons not affected by athetotic, choreiform, or dystonic movements, by a set posture of attention.

In a previous publication [32] it was pointed out that the focusing of attention was accompanied by a certain degree of muscular rigidity. The physiological significance of the muscular rigidity in acts of attention was shown to be the necessary fixation of the relatively central joints of the body and the limbs preparatory to any possibly needed movement of the relatively distal segments.

In the experiments on hyperpnœa this rigidity begins not as an effect of hyperpnœa, but with the act of focusing the attention.

We have seen, however, that in persons affected with athetosis, chorea and dystonia the increased release of muscle tonus is utilized not for the immobilization of the joints, but on the contrary for the exaggeration of the abnormal movements. Even before hyperpnœa has begun, therefore, the concentration of the attention upon the act, involving as it does a release of muscle tonus, has the effect of increasing the movements.

The foregoing considerations furnish a clue to the influence of the emotions in accentuating the fixed postures in the residual spasticity of post-hemiplegic conditions and the abnormal movements in conditions characterized by such movements. The action of an emotion is a concentration of the attention upon a certain thought, or object, or condition. The latter act being inseparable from an increased release of muscle tonus, its result is an enhancement of a pre-existent muscular rigidity or of abnormal movement, as the case may be.

We are now in a better position to understand the effect of hyperpnœa on persons suffering from various forms of paralysis agitans.

X.—The Effect of Hyperpnœa on the Parkinsonian State.

Of the number of cases of paralysis agitans who submitted to the experiment, the following three represent somewhat different clinical types. Other types with general rigidity of a high degree gave inconstant results, owing to the slow and shallow respiratory movements; and the same was true of patients with a considerable degree of mental deterioration. Cases of the latter kind await an improvement in the technique that would make the results of the experiment more conclusive.

Case 22. — B. L., a man aged 48, weighing 148 lb., was a painter by occupation. The disability began eight years ago, with pain in the epigastrium and left shoulder, weakness of the left limbs, and cramps in the calves of the legs. Gradually a tremor developed, more marked in the left upper limb. At present the patient has an immobile expression of the face, a moderate degree of spasticity of the musculature throughout the body, more marked on the left side, and a coarse tremor of the left upper limb. His speech is slow and monotonous. Sensation is normal.

The commencement of the experiment, before hyperpnœa was actually under way, was marked by an increase of the rigidity and of the tremor of the left upper limb.

Two minutes.—The left lower limb becomes affected by a tremor.

Three minutes.—The tremor of the left lower limb ceases. There is a definite increase in the rigidity of the right upper limb.

Ten minutes.—The rigidity throughout the body becomes very much increased, but is more pronounced on the left side. The patient complains bitterly of a pulling pain in the left hip. The pain upon examination is found to be due to the extreme tension of the tensor fasciæ femoris and is immediately relieved by a passive flexion of the limb. The tremor of the left upper limb has increased in amplitude. Upon examination the reason for this is discovered

to be the progressive immobilization by the rigid muscles of the joints of the fingers, wrist and elbow in the order named.

Fifteen minutes.—The left upper limb is held in a semiflexed position, is exceedingly rigid and executes oscillations of large amplitude from the shoulder-joint. All tendon reflexes are very much diminished.

Twenty minutes.—The tremor of the left upper limb ceases. A tremor appears in the calf musculature of the right leg. A coarse tremor affects the right upper limb.

Twenty-five minutes.—The coarse tremor of the left upper limb has returned. When the arm biceps is suddenly and tightly grasped, the tremor in both upper limbs ceases for about one-fourth of a minute, then returns.

At the end of thirty minutes hyperpnœa was discontinued.

Case 22.—I. L., a man aged 38, weighing 200 lb. In 1920 he had a severe attack of lethargic encephalitis. In 1922 his limbs, especially the upper, became somewhat rigid. Early in 1923 the hands were affected for some weeks by a tremor. At the time of the experiment, in May, 1923, the patient had no tremors, the prominent features of his affliction being slowness of movement, monotony of speech, an expressionless face, a marked hypertonicity of the entire voluntary musculature and mental dullness.

The result of hyperpnœa was as follows :—

Eight minutes.—A rather coarse tremor, lasting for about one minute, now in one now in the other upper limb, and occasionally in the right lower limb, recurring about every half minute.

Ten minutes.—A pronounced Babinski sign is easily elicitable on the right side, the great toe remaining, after the cessation of plantar stimulation, in the dorsal position for about one minute.

Fifteen minutes.—The tremors have ceased; they are replaced by sustained rigidity. Hyperpnœa discontinued.

Two minutes later the Babinski sign could no longer be elicited, the great toe definitely assuming the position of plantar flexion upon stimulation of the sole of the foot.

Case 23.—F. D'A., a young man aged 18, weighing 166 lb.

In January, 1920, he had an attack of encephalitis. In 1921 a tremor began in all the limbs.

At the time of this study the patient's musculature on the left side was rather rigid, the face somewhat immobile, and the left limbs affected by a slight tremor. His speech, however, was not monotonous, the gait not visibly disturbed, and there were no other apparent neurological defects.

At the beginning of the experiment the tremor and the rigidity on the left side immediately became accentuated. After three minutes the entire left side became immobilized so that the body shook as a whole, the left limbs executing oscillations of large amplitude. In the next fourteen minutes the movements became so violent that in order to be able to breathe deeply the patient requested that his left limbs be held tightly against the table.

XI.—Further Interpretation of the Results of the Experiments on Patients with Symptoms of Extrapyramidal Disease.

The exaggeration of the movements at the beginning of the experiment in the cases of paralysis agitans was undoubtedly due to the same cause as the similar increase of the movements in the cases of athetosis, choreo-athetosis and dystonia. The release of muscle tonus which constitutes a part of the mechanism of concentrating the attention had for its immediate result an enhancement of the tremor.

The *continued* increase of the abnormal movements in these cases was of course due to a progressive effect of the noxious agents produced by hyperpnœa upon a nerve-structure rendered susceptible by disease.

Although in the different conditions characterized by abnormal involuntary movements experimented upon different portions of the particular system—presumably the striatal system—may have been involved, it is a certainty that the entire mechanism must have suffered to some extent as well. This is evidenced by the fact that all forms of abnormal involuntary movement were, under the action of hyperpnœa, increased until no movable segment of the body and limbs remained at rest. If disease of the striatal system results in a disturbance of the normal state of rest, then the picture of these patients under the conditions of the experiment was the expression of the most widespread disease of this system possible.

The Appearance of Babinski's Sign during Hyperpnœa.

The appearance of the Babinski sign in Case 22 cannot, in the present state of our knowledge, be interpreted except on the assumption of a slight existent injury to the pyramidal system which became manifest under the action of hyperpnœa. Several cases in which a previously non-elicitable sign of Babinski became elicitable, or in which a doubtful sign of Babinski appeared with greater distinctness in the course of hyperpnœa, have been observed. Two examples will suffice as an illustration:—

Case 24.—R. W., a girl, aged 6¼. The child's mother is suffering from "nervousness," the father has had tuberculosis of the hip joint. One brother is undersized, a sister is left-handed and is affected by a tic. The mother is left-handed, as were the grandmother and great-grandmother on the mother's side. The patient herself is right-handed. She is very impressionable.

About a year ago the patient complained of occasional brief attacks of trembling of the left upper limb. Somewhat later she was shocked by the

death of her grandfather. The same day she had the first two major epileptic attacks. The attacks have recurred since then on the average of once a day. The only neurological abnormalities were a lisping speech and a slight predominance of the left patellar reflex.

Following is the record of the effects of hyperpnœa on this patient :—

Five minutes.—Babinski's sign is easily elicitable on both sides, but is more pronounced on the right.

Ten minutes.—The left hand and fingers execute choreic and athetotic movements. Beginning normal tetany in the left hand.

Fifteen minutes.—The right great toe is spontaneously dorsiflexed. The dorsiflexion becomes, however, more pronounced on plantar stimulation.

Case 25.—J. R., a school-boy, aged 9, was run over by an automobile about a year ago, sustaining a slight depressed fracture in the right parietal region of the skull about 2 in. above the ear. The parents complained of a change in the boy's character since the accident. He became dull, inattentive at school, taciturn, shy, and given to violent outbursts of temper.

Except for a very doubtful Babinski's sign on the left side, neurological examination revealed nothing abnormal. After five minutes of hyperpnœa the entire left side of the body became spastic and a very pronounced Babinski's sign was easily elicited on that side.

The Possible Involvement of the Pallio-pontine System in certain Striatal Diseases.

We have seen that the action of hyperpnœa in athetosis, chorea and dystonia is to increase the movements to the utmost possible extent. The consideration has been urged, that if the abnormal movements in these disorders are caused by disease of different portions of the striate system, then the only explanation possible of the effects of hyperpnœa is a most extensive suspension of function of the entire system as a result of the noxious chemical agent introduced. If, now, the rigidity of paralysis agitans is, like the tremor, caused by disease of a certain portion of the striate mechanism, it might be expected that the suspension of function of the entire system would result in both a great increase of the tremor and a great increase of the rigidity. Yet while such a state of affairs is true of the action of hyperpnœa in paralysis agitans, it is not true of the diseases which are not characterized by rigidity but by abnormal movements only. A reasonable inference is, therefore, that the rigidity of paralysis agitans is not due to the disease of the striate system proper, but to that of another system which is likewise involved. The appearance of Babinski's sign in Case 22 speaks for the fact that a cerebral system in close anatomical relation to the striate system may be involved. And if the pyramidal system may be involved in striatal

disease, then the chances of involvement of the pallio-pontine system are greater still. An involvement of the latter system in striatal disease would not result in a disturbance of volitional movement, except in so far as the movement is hampered by the rigidity; and it would not assert itself by Babinski's sign. On the other hand, the action of hyperpnœa in a disease which involves both the striate and the pallio-pontine system might be expected to be just what it actually is in paralysis agitans—a progressive increase of both the rigidity and the abnormal movement.

The investigations of a number of students of striatal disease, however, have failed to discover any abnormalities of the pallio-pontine system as part of the pathological picture of paralysis agitans. Yet the fibres of the pallio-pontine system are anatomically so closely related to the corpus striatum that one wonders how they can escape uninjured in disease of that organ. The large mass of the pallio-pontine fibres, as it plunges into the corpus striatum, breaks up into a number of fine bundles, the spaces between which are filled with striatal cells and fibres. As the pallio-pontine fibres emerge from the corpus striatum the fine bundles unite and appear once more as a single mass, when, in conjunction with the pyramidal tract, they form the pes pedunculi of the mid-brain. The breaking up of this massive tract into fine bundles in its passage through the corpus striatum has not so far been called in question by anatomists; nor have pathologists, in the study of cross sections of the corpus striatum, considered the effects of such an anatomical arrangement upon the pathological picture.

XII.—Summary.

Voluntary deep breathing results in striking abnormal neuro-muscular phenomena which may be utilized for physiological study as well as for purposes of diagnosis and localization of abnormalities of the central nervous system.

On the basis of more than a thousand experiments the statement is confidently made that the procedure, employed with reasonable care, is harmless. The only condition in which its employment requires considerable experience is epilepsy. The induction of an epileptic attack, minor, major or Jacksonian, by means of hyperpnœa, is however, justifiable by an urgency of diagnosis.

The manifestations of tetany induced by hyperpnœa are, within certain limits, of a definite character in persons with an average normal central nervous system. They are as follows:—

(*a*) When a normal person breathes as deeply as he can without undue discomfort at the rate of twelve respirations a minute, manifestations of tetany become pronounced in from fifteen to thirty minutes.

(*b*) These are usually initiated by a slight and transient tremor of the eyelids and of the facial musculature on one side, generally the right. A few evanescent athetotic movements of the fingers may be considered within the limits of normality.

(*c*) In a few minutes the tremor is replaced by sustained muscular rigidity. The orbicularis muscle of the eye, generally the right, and of the mouth, are as a rule involved. The result is that the palpebral fissure on one side is narrowed, and the lips assume the form of a circle which is pressed close against the teeth. Simultaneous with the onset of rigidity in the face, the hands are similarly affected. The thumb and fingers are extended at the interphalangeal joints, semiflexed upon the metacarpus, and approximated at their ends. In this normal tetanic posture the width of the hand is the smallest possible; hence the name justly applied by the French authors—the "obstetrician's hand."

(*d*) If hyperpnœa is not continued beyond this stage, no rigidity is discoverable in any other parts by inspection or palpation. General hypertonus may, however, be inferred from a slight increase of the tendon reflexes.

(*e*) The subjective sensations are slight dizziness and, in the parts affected by rigidity, tingling and numbness.

(*f*) The primary sensations of gross contact, of pain, of the higher degrees of heat and the lower degrees of cold, are rendered somewhat more acute, and the reactions to stimuli of this order are enhanced. The sensations which imply the exercise of judgment are, on the contrary, rather blunted. The power of attention is somewhat lessened. Such a state of affairs speaks, in a general way, for a diminution of cortical function, a moderate reduction of the conscious state.

The manifestations of tetany induced by the method in question in persons afflicted with defects of the central nervous system exhibit numerous deviations from the foregoing. These affect the time of onset, the extent and duration of the abnormal movements, the incidence of the rigidity in certain parts, the pattern formed by the segments of those parts, and the conscious state. On the whole, it is certain that different slight abnormalities of the central nervous system which are not, under ordinary conditions, manifested by definite signs and symptoms, are signalled during hyperpnœa in a striking manner and

in a number of ways. Some of the phenomena of the experimentally induced tetanic state have been described in the present study; but much work remains to be done before these can be correlated with the amount and nature of the existing damage and its localization in the central nervous system.

The most striking action of hyperpnœa is upon the cerebral cortex. This is inferred from a number of the phenomena produced. Among these phenomena are a release of muscle tonus, the plastic character of the rigid muscles, an over-response to affective stimuli, a diminution of the power to discriminate between the finer grades of stimuli, a weakened faculty of attention, the occurrence of mental states amounting to acute dementia, and of complete unconsciousness.

The degree of susceptibility of different portions of the cerebrum to the chemical changes resulting from hyperpnœa is determined by the relative instability of function of the particular tissue. The function of diseased tissue being relatively unstable, it is suspended with ease under the action of hyperpnœa. Hence the incidence of the rigidity or of the abnormal movements in those muscles the corresponding cerebral elements of which are defective.

Certain activities of the skeletal muscles are under the control of the cerebral cortex to a greater extent than are others. Skilled, that is to say learned, movements are most profoundly affected by conditions which depress the functions of the cerebral cortex. Since the musculature of the hand is the most skilled musculature, it is most involved in the manifestations of hyperpnœa; and of the two hands, the right in right-handed and the left in frankly left-handed persons. A further application of the same principle explains the action of hyperpnœa in causing excessive rigidity in the upper limbs in persons who habitually employ those limbs as a support in the acts of standing and walking. The same explanation applies to the incidence of rigidity in a lower limb of a normal person who, in childhood, was affected with disease on that side; and to other seemingly abnormal manifestations of hyperpnœa occurring in normal persons a part of whose musculature is for one reason or another under the special control of the cerebral cortex.

Of the three cerebral inhibitory motor systems, the pallio-pontine is most affected. This is evidenced by the sustained and progressive muscular rigidity. Even when the amount of rigidity ensuing is considerable, however, a volitional redistribution of tonus in antagonistic muscles with movement as a result is still possible. This indicates that the cortico-spinal system is affected to a less extent than is the pallio-

pontine. In normal persons abnormal involuntary movements of a kind referable to the striate system are few and evanescent; and this may be taken as pointing to the relative stability of the striate system.

In diseases of the cerebrum, however, the manifestations referable to the particular system involved become vastly exaggerated under hyperpnœa. In injury to the pyramidal system, so slight as to escape detection by ordinary means, definite signs and symptoms are observable. Every form of abnormal involuntary movement referable to disorder of the striatal system becomes exaggerated to the greatest possible extent. Mental abnormalities assert themselves in pronounced abnormal behaviour.

In the course of the study the fact has obtruded itself that the state of attention, which is inseparable from the exercise of voluntary hyperpnœa, is of itself productive of the same order of neuromuscular phenomena as that which is brought about by the induced alkalosis of the blood. The question, however, whether the "psychic" state of attention is based upon a chemical change in the blood similar to that of the tetanic state awaits an answer at the hands of the biochemist.

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THE CALCIUM CONTENT OF THE CEREBRO-SPINAL FLUID.

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ALTHOUGH the variations in the calcium level of the serum have lately received a great deal of attention at the hands of biochemists and clinicians, but little work has been done on the lime content of the cerebrospinal fluid.

The presence of vascular calcification in the brain after epidemic encephalitis suggests that interesting variations from the normal are possible in the cerebrospinal fluid. It has been shown that the application of lime salts to the cortex diminishes its excitability, and conversely, calcium precipitating salts, e.g., oxalates, increase cerebral excitability. A knowledge of the calcium content of the cerebrospinal fluid is interesting therefore in such disorders as epilepsy, paramyoclonus and tetany.

The work of Cohen [1] on the inorganic constituents of the cerebrospinal fluid in meningitis suggests that an increased permeability of the cells of the choroid plexus might allow a leakage of lime salts until the calcium level approximates to that in the plasma.

The present article embodies the results of an examination of over 115 specimens of cerebrospinal fluids, most of which were withdrawn from patients with chronic neurological disorders. The objects of this research were (1) to determine the average figure, (2) to note wherever any constant variations occur under particular pathological or physiological conditions.

HISTORICAL.

The early accounts of the calcium in the cerebrospinal fluid are meagre and were mostly carried out on isolated pathological cases.

Then Schmidt [13], who was probably the first to write upon the subject, examined the fluid in two cases of hydrocephalus, and found 15·3 mg. per cent. of calcium in an adult and 7 mg. per cent. in a fœtus. Yvon [15] also estimated the calcium content in the cerebrospinal fluid of a fœtus as 8 mg. per cent. Mestrezat [10] in another case of hydrocephalus found 6·2 mg. of calcium in 100 c.c. of cerebrospinal fluid withdrawn after death. He also estimated the percentage in a mixture of twenty normal fluids, and obtained the figure 7·1 mg. Halverson and Bergeim [6] investigated the calcium level in twenty-six fluids, representing nineteen cases, and in one mixed fluid. The cases included one "normal," six tabetics, one tabo-paretic and four general paretics. With the exception of one case of general paralysis which gave the figure of 6 mg. per cent., all the fluids lay between 5 and 5·3, with the average reading of 5·1. They found that no material difference in the calcium level resulted from repeated drainage of the spinal canal.

Kummer and Minkoff [7] estimated the calcium content of four specimens of cerebrospinal fluid, taken from normal subjects prior to stovaine anæsthesia. Their results placed the normal level at 5 to 5·2 mg. per cent. Mann and Golla [9] examined the lime of the cerebrospinal fluid in twelve epileptics and six non-epileptics. In all cases the figures lay between 8 and 9 mg. per cent. Weston and Howard [14] estimated the calcium in twenty-seven cases of manic-depressive insanity; they obtained an average of 5·2 in the excited cases and 5·4 in the depressed.

Leicher [8] also found that the calcium level was remarkably constant (between 4·7 and 5·7) under varying conditions of intracranial pressure. The figure moreover was independent of the amount of lime in the serum. Depisch and Richter-Quittner [4], as a result of a number of cerebrospinal fluid examinations, place one normal at 2·22 per cent. In a certain number of cases no lime at all was detected; these patients showed clinically a definite chronicity of headache of varying severity. In other cases, the calcium content of the fluid was 2 to 3 mg. per cent. higher than the average; these cases also were characterized clinically by severe headaches. In general terms, they found the proportion of lime to be directly proportionate to the intracranial pressure.

Method.

The method employed has been the usual volumetric one whereby the calcium is precipitated by oxalates, dissolved in sulphuric acid and

titrated against potassium permanganate. The titration is not an easy one and a high degree of accuracy can be obtained only after some experience in the method.

To 5 c.c. of the fluid are added 2 c.c. of a saturated solution of ammonium oxalate. The whole is centrifugalized and the supernatant liquid decanted off. The deposit is washed with a 2 per cent. solution of ammonia and again centrifugalized. This process is repeated three times, the final washing being carried out with distilled water. The deposit is next dissolved in 2 c.c. of normal sulphuric acid and titrated hot against a N/100 solution of potassium permanganate. The end point is marked by a faint pink colour which persists for one minute despite vigorous shaking and heating. Care must be taken whilst titrating not to run in too quickly, and to wait until the colour fades before adding more permanganate. From the burette reading is subtracted the amount of potassium permanganate required to produce an identical colour in a control tube of equal volume. The calculation $\frac{R \times 0{\cdot}2 \times 100 \text{ mg.}}{\text{Number of cubic centimetres of cerebrospinal fluid}}$ gives the percentage of calcium, when R equals the number of cubic centimetres of N/100 KMn_2O_8 solution.

Specimens of cerebrospinal fluid showing blood contamination are discarded. Distilled water is, of course, to be used throughout for washing utensils and tubes, and for making up stock solutions.

Results.

The total number of cases in this present series is 115, comprising 70 males, 41 females and four cases in which the sex was not stated. The ages ranged from infancy to 70 years. The average figure for the whole was 6·22 mg. per cent. The average reading for the males was 6·24 per cent. and for the females 6·14.

Although none of these cases can rightly be termed "normal" subjects, many of them were suffering from neuroses and presented no physical signs of organic disease in the central nervous system. For such cases, numbering ten in all, the average percentage was 6·6. Thirty-eight of the 115 fluids were perfectly normal in all respects—pressure, cytology, protein content, colloidal gold reaction and Wassermann. The average calcium in such fluids was 6·1 mg. per cent.

The figures obtained in various organic nervous diseases will be considered next.

	Number of cases	Average mg. per cent.
(1) Acute anterior poliomyelitis	1	6·8
(2) Progressive muscular atrophy and amyotrophic lateral sclerosis	6	6·1
(3) Disseminated sclerosis	15	6·7
(4) Subacute combined degeneration of the cord ..	6	5·8
(5) Acute epidemic encephalitis	2	6·6
(6) Post-encephalitis	8	5·9
(7) Syphilis of the nervous system (25)—		
(*a*) Tabes	12	6·3
(*b*) Tabo-paresis	2	5·8
(*c*) General paralysis	5	6·8
(*d*) Meningo-vascular syphilis	5	6·4
(*e*) Congenital syphilis	2	5·7
(8) Spinal compression (with a partial Froin syndrome in the cerebro-spinal fluid)	4	7·1
(9) Intracranial tumour	3	6·6
(10) Tetany (4)—		
Acute	1	traces only
Chronic	1	4 (approx.)
Convalescent	2	4 and 5·3
(11) Peripheral neuritis	3	6·4
(12) Meningitis—		
(*a*) Cerebro-spinal meningitis	3	6·7
(*b*) Tuberculous	1	6·6
(*c*) Pneumococcal	1	5·8
(*d*) Post-operative	1	6·6
Total ..	6	6·4
(13) Epilepsy	2	5·6

The Influence of other Factors on the Calcium Content.

The possibility must next be considered of any influence on the calcium of other changes in the cerebrospinal fluid, such as pleocytosis, increased globulin, alterations in the colloidal gold reaction, &c.

(1) *Calcium in the blood.*—An examination of the calcium in the blood and spinal fluid of ten cases has shown that there is no constant ratio between the two factors, when the blood calcium is estimated as a whole.

Blood Ca	Cerebrospinal fluid Ca	Ratio
12·1 ..	4·0 ..	1 : 3·25
18·8 ..	6·4 ..	1 : 2·93
19·0 ..	6·5 ..	1 : 2·92
17·5 ..	6·8 ..	1 : 2·57
17·0 ..	5·4 ..	1 : 2·55
13·8 ..	7·7 ..	1 : 2·22
12·9 ..	7·2 ..	1 : 1·79
11·2 ..	7·6 ..	1 : 1·47
9·6 ..	7·2 ..	1 : 1·33
7·0 ..	5·3 ..	1 : 1·32

(2) *The protein content of the cerebrospinal fluid.*—There is no constant alteration in the calcium level corresponding with an increase in protein as shown in the following table:—

Total protein per cent.	Average Ca per cent.	Total protein per cent.	Average Ca per cent.
0·005	6·8	0·05	7·3
0·01	6·3	0·06	7·3
0·015	6·0	0·07	6·2
0·02	5·9	0·1	5·6
0·025	6·3	0·12	6·8
0·03	5 9	0·15	6·4
0·035	5·9	0·3	5·2
0·04	6·5	0·6	8·0

(3) *The cytology of the cerebrospinal fluid.*—The following tables reveal no relationship between a pleocytosis and alterations in the calcium.

Number of cells	Average Ca per cent.	Number of cells	Average Ca per cent.
0	6·1	15	6·4
1	6·0	20	8·0
2	5·8	32	6·3
3	6·5	45	7·3
4	7·3	51	6·2
5	5·1	87	6·8
6	7·0	96	6·2
7	6·7	125	7·3
8	6·2	130	6·1
10	5·9	140	6·0
11	7·2	220	7·2
12	6·2	"Many"	6·1

(4) *The Wassermann reaction.*—There was no gross alteration in the calcium resulting from a positive Wassermann reaction.

Positive in blood and cerebrospinal fluid	13 cases.	Average	6·1
Positive in blood, negative in cerebrospinal fluid	2 ,,	,,	4·8
Negative in blood, positive in cerebrospinal fluid	5 ,,	,,	6·8
Negative in blood and cerebrospinal fluid	75 ,,	,,	6·1

(5) *Lange's Gold Sol. reaction.*—Here too no parallelity existed.

Paretic curve	6 cases.	Average	6·4
Tabetic ,,	8 ,,	,,	6·3
Luetic ,,	4 ,,	,,	6·1
Meningitic curve	7 ,,	,,	6·1
Normal curve	38 ,,	,,	6·1

(6) *Intracranial pressure.*—In fifteen cases the cerebrospinal fluid was under very definite tension. The average calcium reading in these cases was 6·2.

Discussion.

An investigation into the cerebrospinal fluids of 115 cases has demonstrated that calcium is normally present in varying amounts, the

average figure being 6·2 mg. per 100 c.c. of fluid. All writers are unanimous in placing the normal calcium content at a lower figure in the cerebrospinal fluid than in the blood, but various explanations are offered. Halverson and Bergeim suggest that the lower protein content and greater alkalinity of the spinal fluid are in part responsible for the difference in composition. A more reasonable explanation offers itself by considering the choroid plexus as a filter, selective in nature. Rona and Takahashi [12] were the first to point out that the serum calcium exists in two forms—a diffusible form which is capable of passing through a parlodion membrane and a non-diffusible form, constituting 30 to 40 per cent. of the total calcium. The calcium in the cerebrospinal fluid will therefore correspond to the diffusible calcium of the serum. If the normal figure for the serum calcium be taken as 10 mg. per cent., the amount of diffusible calcium will normally be at 6 to 7 mg. per cent., a figure which corresponds well with the average figure for the calcium in the cerebrospinal fluid. It is improbable that the greater alkalinity of the cerebrospinal fluid plays any part in determining the calcium level, as von Meysenbug, Pappenheimer, Zucker and Murray [11] have shown that the ratio : $\frac{\text{Diffusible Ca in the serum}}{\text{Non-diffusible Ca in the serum}}$ is independent of the hydrogen-ion concentration.

Most of the previous writers have emphasized the constancy of the calcium level in the spinal fluid, although varying chemical methods of estimation have placed the normal percentage at slightly different figures. This point is also brought out in our series, no constant gross deviation from the normal being consistently found in any type of cases, with two exceptions. We have been unable to confirm the observations of Depisch and Richter-Quittner who described a series of cases characterized clinically by chronic severe headaches, and which showed absolutely no lime in the spinal fluid. In our hands, the calcium content has proved to be constant in spite of abnormalities in the protein and cell content and changes in the colloidal gold or Wassermann reactions. The proportion, moreover, appeared to be independent of changes in the intracranial pressure.

Cohen has stated that in meningitis the inorganic compounds which normally occur in greater quantity in the blood tend to rise in the cerebrospinal fluid until the fluid approximates in chemical composition to the plasma. Calcium is apparently an exception to this rule. The explanation probably lies in the fact that the choroid plexus acts similarly to a collodion membrane, which according to Cushny [3] will hold back 30 to 40 per cent. of the total blood calcium, but will let through all the sodium, potassium and other ions.

In four cases of spinal compression, where the cerebrospinal fluid showed a partial loculation syndrome, there was evidence that the calcium level was approximating to that of the blood. This is probably due to the leakage of plasma through the inflamed spinal blood-vessels into the subdural spaces of the cord, together with admixture with lymph from the perineural lymphatics.

Interesting results were obtained in four cases of tetany: In one case, which at the time of lumbar puncture was still in the acute phase, the calcium of the cerebrospinal fluid was reduced to mere traces. In two other cases, convalescent at the time of examination, the reduction in the spinal fluid calcium was slighter (5·3 and 4 mg. per cent. respectively). A fourth case of chronic tetany also showed a definite reduction in the calcium content of the cerebrospinal fluid. The serum calcium in these cases was definitely reduced. These facts bear out the statement of Cruickshank [2], namely, that whilst the total calcium of the blood is lowered in tetany, there is a *relative* increase in the diffusible calcium, sometimes amounting to 94 per cent. of the whole. This would tend to explain why the reduction in the spinal fluid lime should be slight compared to that in the blood.

Although the exact form in which calcium exists in the spinal fluid is still unknown, it is probable that part at least is in combination with the protein. The inter-relationship of the lime and inorganic phosphorus constituents in the cerebrospinal fluid still require elucidation, but it does not appear that the same ratio as in the serum exists between them.

The function of the lime of the cerebrospinal fluid is still obscure; it is doubtful whether it takes any active part in restraining cortical excitability, and its main function is probably to help maintain the pH concentration of the fluid at a constant figure. Post-mortem neuronic disintegration appears to affect the calcium cencentration as it does the inorganic phosphorus, for Genck and Blühdorn [5] found as much as 110 mg. of calcium in the ventricular fluid removed at autopsy in a case of fatal toxæmia.

Summary.

As a result of the examination of 115 cerebrospinal fluids, the normal calcium content is placed at 6·2 mg. per cent. This figure is very constant and is apparently independent of the sex or age of the subject.

No marked and consistent diminution has been found in any nervous disorder other than tetany.

In tetany there is a marked fall in the lime content during the acute phase, the calcium rising during convalescence at a greater rapidity than in the blood.

In cases of spinal compression, where Froin's loculation syndrome is present in the cerebrospinal fluid, the calcium content tends to rise.

The calcium of the cerebrospinal fluid is independent of the intracranial pressure, of the cell and protein content, and of Lange's and Wassermann's reactions.

An examination of the calcium of the cerebrospinal fluid offers no assistance in the diagnosis of neurological disorders.

We beg to express our grateful thanks to Dr. Greenfield who placed every facility at our disposal for working in his laboratory.

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OPHTHALMOPLEGIA INTERNUCLEARIS ANTERIOR: A CASE WITH NECROPSY.[1]

(Paralysis of each Rectus Internus in Lateral Associated Movement, with Preservation of Function of these Muscles in Convergence and of the Function of each Rectus Externus.)

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There are different forms of paralysis of associated ocular movements, and on previous occasions I have written on the paralysis of associated upward and of associated lateral movement [18-21]. The subject which concerns me at the present time is that of an unusual form of paralysis of associated lateral movement, ophthalmoplegia internuclearis anterior, and the case I report is, I believe, the only one of this type with necropsy. It is, perhaps, well to have clearly in mind the different types of associated lateral ocular palsy. Ernest Fuchs [6], in his textbook, makes the following classification of this form of ocular paralysis.

(*a*) Neither eye, when attempting to follow an object that is moving to one side, say the right, can move beyond the middle line. But the left eye can move to the right when converging on an object which is brought in towards the eyes in the median plane (retention of convergence).

(*b*) Neither eye can follow an object that is carried to the right, provided both eyes are open, but the left eye can follow the object to the right if the right eye is covered. This is really the same case as (*a*), the movement inwards of the left eye when the right eye is covered being simply a movement of convergence (Jeffries, Moebius).

(*c*) The right eye can follow an object that is moving to the right, but the left cannot. The left eye, however, can move to the right in performing convergence. This condition, which may be called conjugate hemiparalysis, is thus distinguished from a paralysis of the left internus in which the left eye can move inwards neither when

[1] Read before the American Neurological Association, June 6, 1924.

converging nor when attempting to make a conjugate movement to the right.

(*d*) Both interni may be paralysed for conjugate movement (Wilbrand and Saenger).

(*e*) Neither eye can follow an object which is carried to the right, and the left eye, moreover, cannot move to the right when attempting to converge (combined paralysis of lateral movement and convergence).

Paralysis of lateral movement is sometimes bilateral, i.e., both eyes fail to follow an object that is carried either to the right or to the left, although it may be that both can still converge.

The case which I here report belongs to types *c* and *d* of Fuchs's classification.

The patient was in the service of Dr. Alfred Stengel, at the University Hospital, and I am indebted to him for permission to report the case and to Dr. Baldwin Lucké for the pathological material.

Mrs. S. J. W., aged 46, was admitted to the University Hospital, November 13, 1923, and died November 23, 1923. The clinical diagnosis was mitral stenosis, auricular fibrillation, failure of compensation, infarct of both lower lobes of the lungs, and a vascular lesion in the pontile tegmentum.

She complained of shortness of breath, weakness, diplopia and difficulty of speech.

The patient suddenly on November 4, 1923, experienced a feeling of fullness in the head, her eyes seemed to bulge, and at the same time she felt a sensation of numbness in the left half of her face and tongue, in her left upper limb, left side of trunk and left lower limb. She was unable to talk with clearness since this attack and has been confined to her bed. She had much dyspnœa, was very weak in all parts of her body and had diplopia.

She had been apparently well before the attack on November 4, except that she had been subject to colds and a cough of a dry unproductive nature. The coughs were usually associated with "spells of the heart." She gave no history of hæmoptysis or night sweats. She became very dyspnœic on exertion and when lying flat on her back. She had had palpitation of the heart, but no œdema and no cyanosis. She did not use alcohol. Her blood pressure was 145—90.

When she came into the hospital she was more comfortable sitting up in bed on account of the dyspnœa. She was breathing rapidly and with great effort and continual grunting expiration. She was entirely rational and understood requests made to her, but was unable to talk distinctly, stumbled in her speech, and had difficulty in saying one word after another, although she knew what she wanted to say. She appeared to be very ill. No weakness of the facial muscles could be detected. The pupils were large and the irides reacted promptly to light and in convergence. There was no ptosis, nystagmus or exophthalmos. She had distinct paralysis of both internal recti muscles in

making lateral movements, but no other extra-ocular palsies could be detected. The tendon reflexes were about normal in the right limbs, but the patellar and Achilles reflexes were a little exaggerated on the left side. She did not have a positive Babinski sign.

Dr. de Schweinitz examined the patient November 13, and found: "Marked divergent strabismus with practically complete loss of internal rectus action in both eyes for right and left lateral movements, but in the associated movement of accommodation both internal recti act. Other movements apparently are normal. No hemianopsia. Both pupils are large but react to light normally. Eyegrounds are normal." There was probably paralysis of the left superior oblique muscle which on account of the patient's condition would have been difficult to detect. The urine was normal.

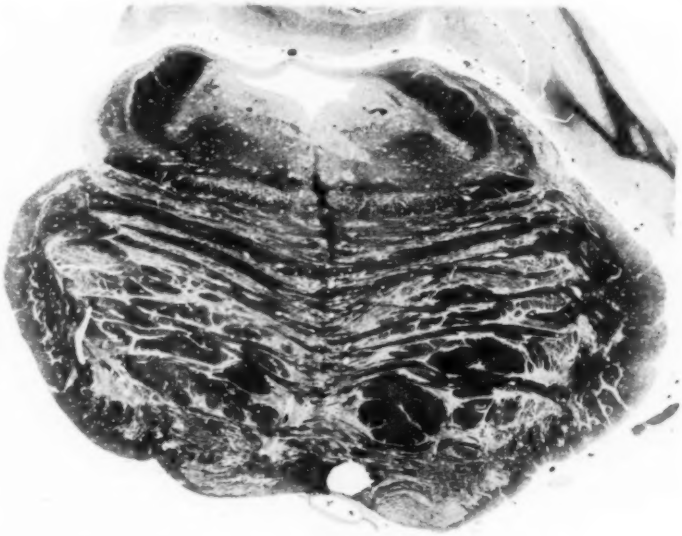

FIG. 1.—A section close to the lower limit of the softening.

An examination on November 13 failed to reveal any hemiparesis, although there was a history of previous hemiparæsthesia and weakness. Lobar pneumonia was diagnosed on the 14th, with consolidation of the right lower lobe. The blood count of red blood cells was normal, but she had 20,000 white blood cells November 14. A few hyaline and light granular casts were found in her urine on November 15. The blood Wassermann was negative.

I saw her on November 22, but she was too ill for examination and was stuporous. My diagnosis was a lesion in the posterior part of the pons

implicating the posterior longitudinal bundle of each side, of vascular origin, with softening.

She became progressively worse, the paralysis of the internal recti mentioned persisted, and she died of heart failure on November 23.

On microscopical examination of serial sections I found as follows: Each abducens nucleus was entirely normal, the nerve cells were numerous and in good condition, although here and there one might be found which showed some degeneration but not more than would occur

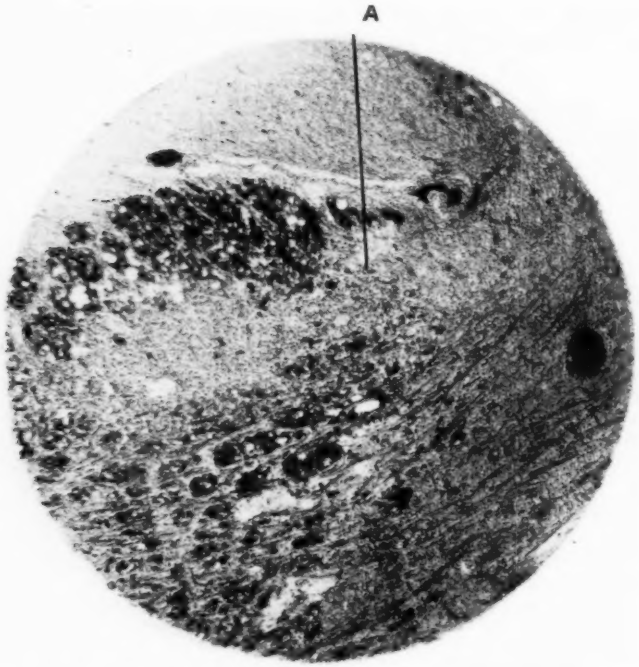

FIG. 2.—The same section as shown in fig. 1, under higher power. Degeneration of the posterior longitudinal bundle of one side, A.

in a normal specimen. The intrapontile fibres of the abducens nerve were normal both in structure and number. There was no softening anywhere near either abducens nucleus. The posterior longitudinal fibres stained well with Weigert's hæmatoxylin method below the area of softening. The patient had lived only nineteen days after the lesion developed. The softening began (figs 1, 2 and 3) about at a level represented in sections corresponding to Obersteiner's fig. 172 [12].

At the level of the corpora quadrigemina the softening implicated the tegmentum on each side of the raphé to about the posterior fibres of the pryamidal tracts. Small hæmorrhages were also found here around the vessels and also apart from the vessels within the tissues.

The left nucleus trochlearis was destroyed in its lower part and much degenerated in its upper part, where the nerve cells were much less numerous, and some of them showed chromatolysis, displacement of the

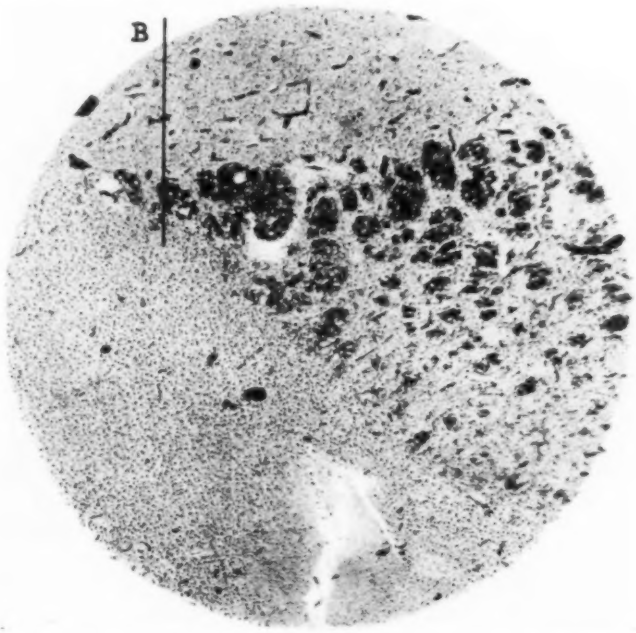

FIG. 3.—The same section as shown in fig. 1, under higher power. Degeneration of the posterior longitudinal bundle of the other side, B.

nucleus and swelling of the cell body. The area of softening at the level of the nucleus trochlearis destroyed most of the left posterior longitudinal bundle and invaded the ventral part of the right posterior longitudinal bundle. It implicated the tissue on each side of the raphé and extended forward to the interpeduncular space, destroying all the structures in this part.

The nucleus oculomotorius was not invaded by the softening on either side, and these nuclei appeared intact at all parts. Their nerve

cells were in normal number and well preserved, and did not show "reaction at distance." Some of the nerve fibres from each nucleus passed through the degenerated area, and no medullated fibres were seen in the degenerated area. The area of softening was small where the nucleus oculomotorius on each side had its greatest development, and was confined to the region about the raphé, so that many fibres of these nuclei were not affected, and the area of softening disappeared below the region where most of the oculomotor fibres have their exit.

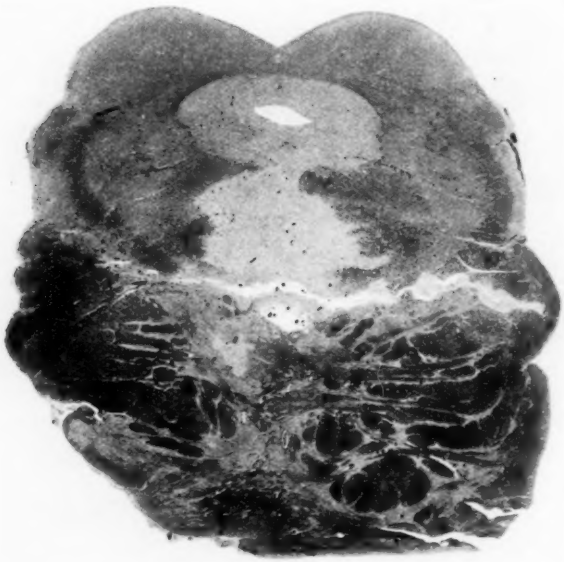

FIG. 4.—Section at the level of the nucleus trochlearis. Degeneration of each posterior longitudinal bundle.

Some of the small blood-vessels of the cerebral peduncles were filled with clots of red blood-cells, and many small hæmorrhages were found about the vessels and in the perivascular spaces of this region.

Many small vessels in the cerebral peduncles, pons, and medulla oblongata were filled with thrombi consisting of polymorphonuclear cells; even in the centrum semi-ovale a few similar vessels were found.

The softened areas consisted of masses of fatty granular cells (gitter cells), and about these areas were numerous much swollen axis cylinders.

The interesting clinical features of this case were the vascular attack without paralysis of the limbs, and the ocular palsy.

The attack was of sudden onset. The patient had a sensation of fullness of the head, with a feeling as though the eyes were bulging, and with numbness of the entire left side. The distinctness of speech was affected by the attack. The ocular condition was paralysis of the internal rectus muscles in associated lateral movement, with preservation of the convergence movement of these muscles and with preservation of the movements of the external rectus muscles.

FIG. 5.—The same section as shown in fig. 4, under higher power, showing degeneration of each posterior longitudinal bundle and of the left nucleus trochlearis.

The patient was difficult to examine, as her mentality was affected. Dr. de Schweinitz found the eyes markedly divergent, and this could be explained, in his opinion, only by the preservation of the action of the external rectus muscles. There was practically complete loss of the action of the internal recti in their associated lateral movements, with

preservation of their associated movements in convergence at the time of the examination made by Dr. de Schweinitz.

Dr. E. Dench, the intern on the service, made the physical examination of the patient on November 13, and was absolutely positive that she could innervate each external rectus muscle. His note written at the time of his observation reads: "Has distinct paralysis of both internal recti in making lateral movements. Can make out no other extra-ocular palsies." Dr. Edward Rose made a similar observation.

The patient lived nineteen days after the onset of her attack, but was in the hospital only ten days, and developed lobar pneumonia.

The region of the oculomotor nucleus is not an uncommon site of vascular occlusion. I reported a case of this kind with necropsy in 1913 [22]. An excellent explanation for this occurrence is given by Shimamura [16]. According to him there is a vessel of considerable size on each side of the raphé both in the pons and in the cerebral peduncles. The region of the oculomotor nucleus is especially liable to vascular disturbances, because it is supplied by blood coming from two systems, viz. the carotids and the vertebral arteries, and the blood currents from these two systems, coming from opposite directions, meet where the vessels leave the base to penetrate the brain. These vessels entering along the raphé have a perpendicular course and are end vessels. Shimamura believes that in any fall of blood-pressure a lack of blood is especially liable to occur in the region of the oculomotor nucleus.

Paralysis of lateral associated ocular movements is supposed to have been first observed by Foville (1859) and since then has been observed by many, but it seems to have been Féréol, as Freeman [5] has pointed out in his excellent paper, who fully recognized the syndrome.

Lewandowsky [9] mentions that v. Monakow concluded from the reported pathological findings that the lesion producing this ocular disturbance must implicate the abducens nucleus and the posterior longitudinal bundle. Siemerling believed that destruction of the abducens nucleus alone is not sufficient to cause paralysis of lateral associated ocular movement (Blicklähmung). He was referring to the form of palsy in which both eyeballs cannot be moved together beyond the middle line toward the side of the lesion in the pons, and yet the internal rectus, which is incapable of function in lateral associated movement, is capable of function in convergence. In a few cases of paralysis of lateral associated ocular movements the convergence power seems to have been lost also, and an example of this is attributed to Bleuler.

Lutz [11] has written one of the most recent papers on paralysis of associated ocular movements and gives evidence to show that the fibres for the associated movement of the rectus internus cannot arise in the nucleus abducens. He states that some authors accept a supranuclear centre in the pons, and believe that from this fibres pass to the nuclei of the internal and external recti muscles. This centre is supposed to be located in the grey matter of the aqueduct (v. Monakow, Bernheimer, Lewandowsky) between the nucleus abducens and the nucleus oculomotorius, nearer to the former. The majority of writers on this subject accept this centre: for example, Bing, Wilbrand and Saenger, Holmes, Cantonnet, Grasset, Julin, Raymond and many others; an exception to this, he states, is found in the views of Dejerine and Spiller. He mentions that it is a fact that no one so far has been able to find such a centre, and he questions whether there is any necessity for accepting such a centre. We raise and allow both eyelids to fall simultaneously, we swing both upper limbs from before backward, and find no necessity for assuming a supranuclear centre for such movements. This is a view with which I am in entire sympathy.

The centre for lateral associated movement has been supposed by some investigators, as has been said, to be in the abducens nucleus, but Wilbrand and Saenger mention that in paralysis of this movement the abducens nucleus was intact in the cases of Senator, Bristowe, and Quioc; and the cases of Garel and Hunnius also are mentioned as showing no lesion of this nucleus itself. It may be well to examine these cases critically.

Senator's case [15] was without necropsy, at least no mention is made of a necropsy in the report of the case.

Bristowe's case [2] was without microscopical examination.

Quioc's [13] case was one in which a tumour was found at the necropsy, which from its situation to the naked eye was said to leave the abducens nucleus uninvolved, but was supposed to implicate the abducens nerve. There seems to have been no microscopical study in this case.

Garel's case [7] did not show integrity of the abducens nucleus, as no microscopical sections were studied. The lesion was an area of softening. The report of Hunnius' case I could not obtain.

Lewandowsky [9] remarked that one must assume theoretically that from interruption of the tract between the level of the abducens nucleus and the corpora quadrigemina paralysis of the internus in attempted lateral movement of the eyes occurs without abducens

paralysis, i.e., paralysis of lateral associated ocular movement of only one eye, with preservation of convergence. He refers only to the cases of Bielschowsky and Fischer, but states that no necropsies have been obtained in such cases. This statement was made in 1910.

Bielschowsky [1] stated that A. v. Graefe considered it almost unbelievable that the rectus internus could be paralysed only for lateral movement of the eyeball when the function of the rectus externus of the other eyeball was preserved. To refute this opinion in part Bielschowsky reported his case.

The patient, aged 45, who had fallen and struck his head in the occipital region, had his right eye in divergence about 20°. In looking to the left the left eye moved normally, but the right eye moved only to the middle of the palpebral fissure. The right eye had normal abduction, but the associated movement of the left eye to the right was two-thirds behind normal. The convergence reaction was almost normal. Elevation of the eyeballs was almost entirely lost, downward movement was retained. Recovery of ocular function occurred. The lesion was supposed to be minute hæmorrhages in the oculomotorius nuclei.

Another case reported by Bielschowsky is one to which Fischer alludes. It was regarded as a case of encephalitis of the pons and presented paralysis of one internal rectus in lateral movement with fairly preserved convergence reaction.

Fischer [4] regarded his own case as one of multiple sclerosis. The patient was a woman, aged 42. The ocular symptoms developed suddenly. During more than three weeks she had paresis of the right rectus internus in lateral movement without any disorder of the muscles of the left eye; the left rectus externus was entirely normal, indeed it seemed to be over-innervated because of the paresis of the right rectus internus in lateral movement. The left eye in looking to the left went outward with a strong movement. There was no disturbance of ocular movement upward, downward, or toward the right. Convergence of both eyes was entirely normal. The disturbance disappeared in less than four weeks.

The case described by Wilbrand and Saenger [23] was as follows: A woman, aged 23, previously healthy, had a peculiar sensation in her head and two days later awoke with diplopia. The eyes were in divergence. Each eye tested separately could not be moved inward beyond the median line, while convergence reaction, especially in looking downward, was very prompt. A symmetrical paresis of both superior

recti existed. The pupils were equal and reacted promptly to light. Accommodation and the ophthalmoscopic findings were normal. The condition was regarded as early multiple sclerosis. Recovery from the ocular palsy occurred.

Lutz says that Wilbrand and Saenger reported two cases of this type. The other case probably should not be included. Wilbrand and Saenger report it separately from their typical case (p. 65), although in the same volume, and speak of it as an example of isolated paralysis of the rectus internus, which they state has not been reported except in this case of theirs. They evidently do not regard it as similar to the case described above. It was one in which each rectus internus was paralysed in binocular or monocular testing, and no mention is made of the condition of convergence. Recovery occurred. The diagnosis was encephalitis of the pons, probably following influenza.

Lhermitte [10] employed the term "internuclear paralysis" of the ocular muscles, but such a lesion was demonstrated by Raymond and Cestan. Lutz [11] suggested the additional differentiation into opthalmoplegia internuclearis anterior and ophthalmoplegia internuclearis posterior. By the former is meant the condition in which only the rectus internus fails to function in lateral movement and has preserved convergence power. By the latter is understood only a paralysis of the rectus externus in lateral movement, and the accompanying symptoms must indicate whether this is a supranuclear palsy or an infranuclear palsy. Priestly Smith [17] observed three cases of this type, according to Lutz. The three patients had paralysis of left lateral associated movement without impairment of convergence. Improvement occurred, so that the left rectus externus remained paralysed, but the right rectus internus became entirely normal. This indicated that the paralysis of the left rectus externus was not infranuclear. A similar case he says has been reported by Wilbrand and Saenger.

Lutz [11] reported a case of ophthalmoplegia internuclearis anterior without necropsy, and made the diagnosis of epidemic encephalitis.

Gordon Holmes [8] makes a very brief reference to his cases. He says merely that he has seen isolated paralysis of the rectus internus in lateral movement, though this muscle contracted in convergence. In his two cases the symptoms made it probable that the dorsal longitudinal bundles were interrupted in front of the sixth nucleus, but the sites of the lesions could not be confirmed by autopsy.

These are the only clear cases of ophthalmoplegia internuclearis anterior I have been able to find, and they are all without necropsy.

The case of Raymond and Cestan [14] also gave evidence that von Monakow's view regarding the necessity of implication of the abducens nucleus in paralysis of lateral associated movement is incorrect. In this case, reported by Raymond and Cestan, the patient, a man aged 60, had the eyes in the median position without permanent strabismus: he had paralysis of associated lateral movement, especially toward the right. Upward, downward and convergence movements were well preserved. A large tubercle was found in the tegmentum of the upper part of the pons. The abducens and oculomotorius nuclei were intact, and the nerves from these nuclei were unaffected.

The case was regarded by these authors as proviug the possibility of paralysis of associated lateral movement from an internuclear lesion without affecting the nuclei of the ocular nerves. It may be well to note that the lesion was a large tubercle, and it is possible that some disturbance of function was occasioned by pressure on the abducens nucleus.

Brouwer [3] has studied the localization for convergence. According to him, Knies, in 1891, assumed that Perlia's nucleus was the nucleus of convergence. This view was supported by Stuelp and Majano. Von Monakow assumed that the rectus internus must have two nuclei: one which associated it with the rectus internus of the other eye in convergence; and the other which associated it with the rectus externus of the other eye in conjugate lateral movement of the eyeballs. He placed the convergence nucleus in a frontal position in the nucleus oculomotorius without speaking of Perlia's nucleus. Edinger also assumed a frontal position for the nucleus of rectus internus. Brouwer also supports Knies's view, and concludes that not only Perlia's nucleus but more caudal cells in the region of the raphé also serve convergence. These cells appear in phylogenetic development when the position of the eyes in the head makes convergence possible. In this manner Perlia's nucleus is phylogenetically the youngest portion of the nucleus oculomotorius. Its relation to the Edinger-Westphal nucleus is to be explained by neurobiotaxis (Ariëns-Kappers). Its cells approach in phylogenetic development the Edinger-Westphal nucleus, which serves for accommodation and contraction of the pupil in association with convergence movement.

Convergence was preserved in my case because the anterior part of the nucleus oculomotorius was not affected by the area of softening.

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ON THE FUNDAMENTAL PROCESSES IN THE CORTEX OF THE CEREBRAL HEMISPHERES.

II.—On the Principal Cortical Elements in the Arcs of the Individual Reflexes.

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I.—The Cortical Composition of the Reflex-Arc in Motor Individual Reflexes.

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III.—The Rôle of the Cutaneous Analyser, the Motor Analyser and the Motor Apparatus in the Individual Reflex.

IV.—Conclusions.

The method of investigation was the same as that described in the first article [1], and the experiments were carried out on the same four dogs—"Bob" "Moura," "Bezoukh" and "Beli."

I.—The Cortical Composition of the Arcs of Motor Individual Reflexes.

In the course of the formation of an individual motor reflex it is often observed that this reflex is similar to the one obtained to electrical stimulation (Faradic shocks). In a series of experiments on both these reflexes the animal groans and moves its limbs and the whole body disorderly. In another series the animal raises only the limb that is stimulated. This similarity shows that the central elements through which the reflex to electrical stimulation is evoked participate in the formation of the individual reflex. We must now investigate what elements are common to both these motor reflexes.

Electrical stimulation excites the cutaneous analyser and also raises its excitability. Individual stimuli also excite a certain section of the cortex, and raise its excitability too. Therefore if electrical stimuli regularly coincide with some indifferent stimuli a temporary connection must be formed between the cutaneous analyser and the analyser that receives the individual stimulus.

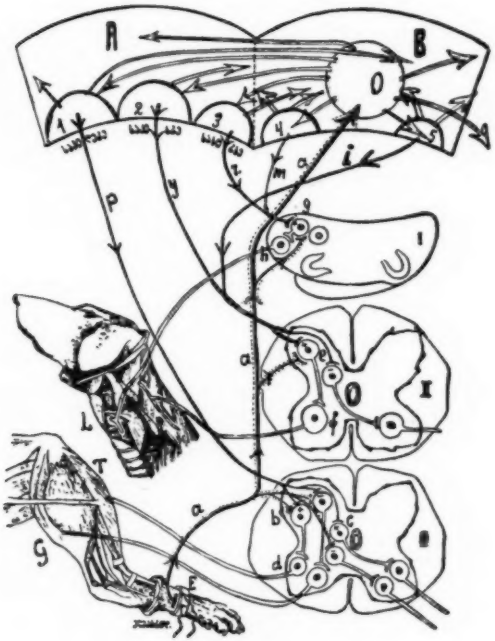

FIG. 1.

Fig. 1.—A semi-diagrammatic figure of the nervous paths and centres through which the excitation spreads on electrical stimulation of the skin of the hind-limb of a dog. (A.) The motor analyser in the cerebral cortex. (B.) The cutaneous analyser. (O.) The part of the latter which is excited by the electrical stimuli. (1) The cortical motor apparatus for the hindlimb in the motor analyser. (2) The cortical apparatus for the neck in the motor analyser. (3) The cortical motor apparatus for the vocal reaction in the motor analyser. (4) The same for the neck in the cutaneous analyser. (5) The same for the vocal reaction in the cutaneous analyser. (i) The medulla oblongata. (ii) The cervical portion of the spinal cord. (iii) The lumbar portion of the spinal cord. (*a*) The afferent path that transmits the excitation from the stimulated limb to the spinal cord and to the brain. (*b*) The co-ordinating apparatus of the ipsilateral flexion reflex. (*c*) The same for the contralateral extension-reflex. (*d*) The motor neurons to the tibialis anticus and gastrocnemius muscles. (*e*) The co-ordinating apparatus of the neck. (*f*) The motor neurons to the neck muscles. (*g*) The co-ordinating apparatus of the larynx. (*h*) The motor neurons to the laryngeal muscles. In the co-ordinating apparatus the plus sign (+) denotes the excitory neurons and the minus sign (−) the inhibitory ones. The arrows show the innate connections between these parts of the nervous system, and the direction of the nervous processes in these connections on stimulation of the hindlimb. *p*, *y*, *r*, *m*, *i* indicate fibres of the pyramidal tracts.

Further, electrical stimuli provoke through the cutaneous analyser an excitation of definite motor apparatuses in the cortex and raise their excitability (see fig. 1). This creates the conditions for a reciprocal action between these apparatuses and the focus excited by the individual stimulus. A temporary connection is therefore established with a point of the cutaneous analyser, as well as with the cortical motor apparatuses of the limbs, of the orientational reaction of the head and of the vocal reaction.

Thus, in addition to the analyser of the individual stimulus and the cutaneous analyser which is affected by the electrical stimulus, a series of cortical motor points must participate in the arc of the individual motor-reflex. I believe these motor points differ functionally from those which receive the excitations. The co-ordination of movement is not, however, determined in the cortex, but in the subcortical parts of the brain and in the spinal cord. (Hering and Sherrington [2] and others.) The co-ordination of the motor individual reflex must therefore depend on subcortical parts of the nervous system which act under the influence of impulses issuing from the cortex (fig. 1).

II.—On the Formation of Individual Motor Reflexes to Proprioceptive Stimuli of Secondary Origin.

The arc of the individual reflex is not confined to these elements of the cortex. We know that the slightest movement of a limb or of any part of the body evokes a whole series of secondary proprioceptive stimuli from the joints, muscles and tendons. All these affect the cortex, evoking excitations in it, and in addition increase the excitability of parts of the motor analyser. In Pavlov's laboratory the term motor analyser is given to that area of the cortex which receives stimuli from the muscles, tendons and joints. Consequently each individual stimulus is combined not only with electrical stimuli, but also with a whole series of secondary stimuli. A temporary connection must be therefore established between the cortical focus of the individual stimulus and the foci of these secondary stimuli in the motor analyser.

As I have shown above, an excitation of the cutaneous analyser and of a definite motor apparatus occurs in both the individual and electrical reflexes. The excitation of the cutaneous analyser and of the motor apparatuses proceeds simultaneously with the excitation of the motor analyser by secondary stimuli. It follows that a certain

reciprocal action must also occur between the cutaneous analyser and the motor apparatus on the one hand, and the motor analyser on the other, which leads to the formation of a temporary connection between them.

These statements can be deduced directly from observations. In the first place when the individual stimulus is combined once only with a short electrical stimulus the individual reflex often outlasts the individual stimulus; in some cases the reflex is maintained a considerable time after its cessation. As this stimulus could have provoked a reflex only during the period of its own activity, the after-effect in the

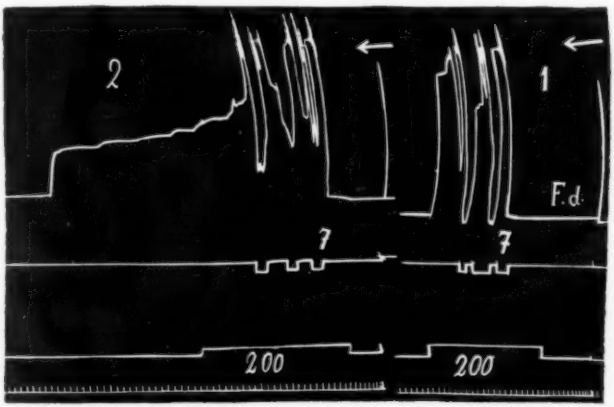

FIG. 2.

Fig 2. "Bob," December 7, 1916.—The first day of an experiment with a thrice repeated combination of electrical stimuli to the right forelimb with a sound of 200 vibrations per second. Record 1 shows the first combination and Record 2 the fourteenth, 1 hour and 5 minutes after it. In the first combination the first and second electrical stimuli evoked reflexes of short duration, and the third one evoked one with an after-effect of about 5 seconds. In the fourteenth combination each electrical stimulus evoked a reflex with an after-effect; after a third stimulus this lasted 30 seconds.

individual reflex may be attributed to the action of secondary individual stimuli of muscular and articular origin. This conclusion is made more probable by the fact that when each individual stimulus is combined with an electrical stimulus the after-effect occurs regularly, and may last several seconds and even minutes.

In order to demonstrate clearly the origin of this after-effect in the individual reflex, I will give a detailed description of a characteristic instance of the formation of a reflex to electrical stimuli repeated with each individual stimulus. A reflex on "Bob" was first formed to a sound of 200 vibrations per second by combining it with a single short electrical stimulus. Then, in order to lengthen the individual reflex, the sound was combined with an electrical stimulus applied three times;

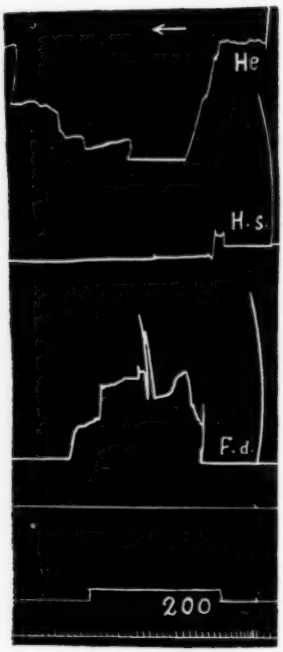

FIG. 3.

Fig. 3. "Bob," December 8, 1916.—The second day of the experiment with the combination thrice repeated of a sound of 200 vibrations per second, with an electrical stimulus to the right forelimb. The sound was applied after fifteen combinations. It elicited an elevation of the limb which lasted the whole time of the sound, that is 22 seconds (bottom curve). At the same time there was a strong orientational reaction on the head (top curve) and a slight movement of the left hindlimb (middle curve).

each stimulus lasted 1 second to 3 seconds, and was repeated three times every 2 seconds to 3 seconds while the sound lasted. After

several combinations the character of the individual reflex, as well as that of the reflex to the electrical stimulus, changed completely. In the first combination, after the reflex movement to the third electrical stimulus, a new movement of short duration was observed. In the following combinations this new movement became longer, and it occurred also after the second and first stimuli (see fig. 2 in which the first and the fourteenth combinations of this experiment are shown). This after-effect appeared independently of the sound, and the repeated electrical stimuli produced the same effects without the sound as with it. Further, even when only a single electrical stimulus was employed

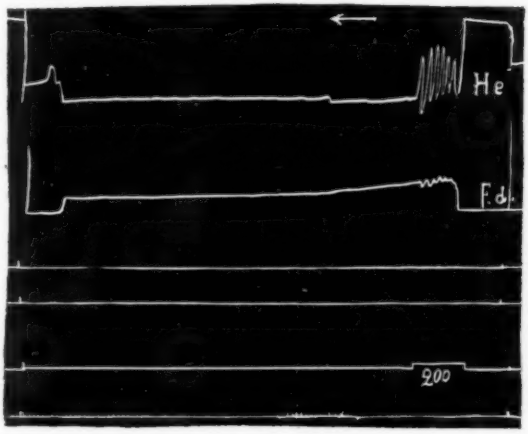

FIG. 4.

Fig 4. "Bob," November 20, 1917.—An individual reflex of the right forelimb to a sound of 200 vibrations per second. The sound lasted 11 seconds. The reflex persisted about 1 minute after the cessation of the sound (bottom curve). Simultaneously an orientational reaction on the head (top curve) occurred.

the reflex did not cease immediately on the cessation of the stimulus, but persisted for several seconds, as is seen in fig. 8.

Further, even on the first day the effect of the individual sound changed. The individual reflex to single combinations was usually of short duration; sometimes it was composed of a series of rapid movements which rarely lasted 10 seconds to 20 seconds. This occurred notwithstanding a large number of combinations (up to 500)

Now, after only fifteen combinations, a sound of 200 vibrations regularly evoked a long-lasting effect that continued for the duration of the sound, for more than 20 seconds (see fig. 3). Later, the usual sound, which lasted 3 seconds to 10 seconds, produced an after-effect persisting several seconds, as is seen in fig. 4.

Thus, if while the sound lasted the electrical stimuli succeeded each other rapidly, the reflexes both to the electrical stimulus and to the sound altered. Observations showed that the reflex to the sound changed only in so far as it was affected by the electrical stimuli. If a new reflex of the same limb is formed during this time, and if it is combined with a single electrical stimulus, it may take the form of the reflex to the sound of 200 vibrations per second, or of the reflex evoked by an electrical stimulus alone.

There is no difficulty in understanding the origin of such an alteration of the reflex when we pass from a single electrical stimulus to repeated stimuli. When an electrical stimulus is repeated at the same time as the individualized stimulus the conditions for the formation of a secondary reflex are much more favourable than when it is single. In repeated stimulations strong secondary stimuli resulting from the preceding motor effect are combined with a new electrical stimulus. As we know from the work of Pavlov's laboratory a greater intensity of the individualized stimulus, as well as a temporary succession in the combinations (first the individual and then the principal active stimulus) has an important influence on the rapidity of the formation and on the further development of the individual reflex (Tichomiroff [4], Krestovnikoff [3]).

When individual stimuli are combined with electrical stimuli, secondary stimuli only once precede the electrical stimulus, and even this happens only if the latter is applied during the individual reflex. In the latter case the intensity of the secondary stimuli excited by a comparatively weak individual reflex must be feebler than in the case of a thrice-repeated electrical stimulus, since they are then also excited by the movements evoked by the electrical stimuli.

Several examples could be cited to show that secondary stimuli of muscular and articular origin are the most active exciters of a new motor reflex. Thus, in the course of experiments with a thrice-repeated electrical stimulus it frequently happens that directly after the lowering of the limb which had been previously raised in response to an electrical stimulus, a fresh elevation of that limb followed without a fresh electrical stimulus. This was observed in all the dogs when weak stimuli were

employed, and in "Bezoukh" with stimuli of any strength. In the other dogs stronger stimuli produced a reflex with a persisting after-effect.

Fig. 5 illustrates two experiments conducted with stimuli of different strengths, the coils being separated 8 to 10 cm. In both the limb was lowered immediately after the cessation of the stimulus, and this was followed by a secondary elevation.

The following is a more demonstrative fact. If an electrical stimulus is applied to the limb repeatedly while its flexors are completely relaxed, every relaxation of flexion of this limb in subsequent experiments will be accompanied by a groan, a strong movement of the head and by

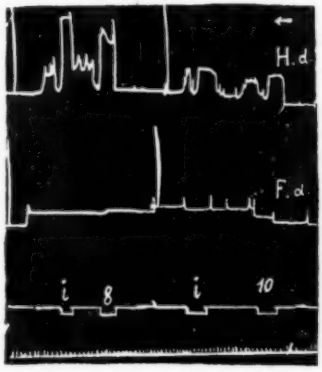

FIG. 5.

Fig. 5. "Bezoukh," June 12, 1918.—An illustration of the second elevation of the right forelimb to electrical stimuli of different strengths. Further explanations are given in the text.

repeated strong flexion of the limb. This experiment illustrates very well the fact that the individual reflex to secondary stimuli is conditioned by the formation of temporary connections between the motor analyser and the cutaneous analyser. Such an experiment is shown in fig. 6.

It is easy to prove that this after-effect really represents an individual reflex and is not an after-effect of spinal origin, for when it is elicited by an individual sound or by an electrical stimulus, it is, as the ordinary individual reflex, easily modified by unusual stimuli. If an unusual stimulus capable of removing the primary individual reflex is applied during the after-effect, it arrests this even more easily. In fig. 7, for

instance, the unusual stimulus, a bell, was repeatedly applied during the persistence of the individual reflex to the sound of 200 vibrations, and it produced a negative effect on the reflex during the sound and after it.

Fig. 8 shows the negative action of the bell on the after-effect of a reflex to an electrical stimulus.

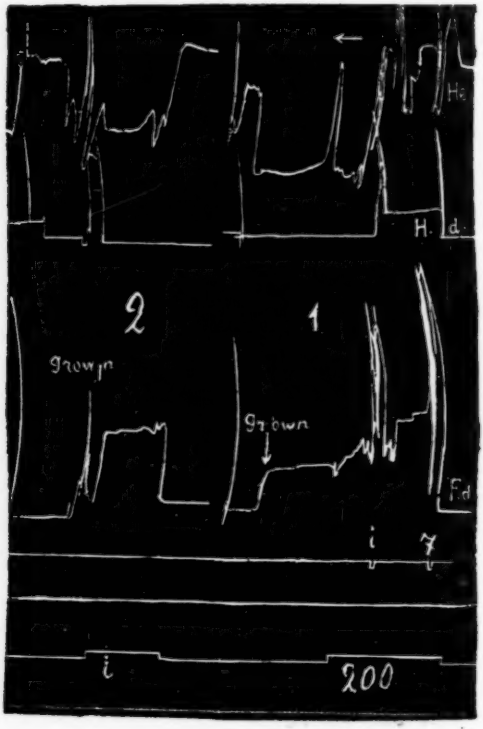

FIG. 6.

Fig. 6. "Bob," January 18, 1917.—The formation of an individual reflex to lowering of the right forelimb. In the first experiment the after-effect of the reflex evoked by an electrical stimulus simultaneous with the individual sound (200 vibrations per second) was combined with a new electrical stimulus at the moment of lowering of the limb. In the second experiment the individual reflex became feebler immediately after the cessation of the sound; the limb dropped suddenly; later it rose again and there occurred strong movements of the hind-limb (middle curve) and of the head (top curve) and groans, as if a strong electrical stimulus had been applied.

There can therefore be no doubt that the reflex after-effect which manifests itself in reflexes to individual and to electrical stimuli represents a typical individual reflex to secondary stimuli of muscular and articular origin.

The influence of secondary individual reflexes on the reflexes to any individual stimulus is undoubtedly very great. The fact that it is impossible to form a primary individual reflex without secondary ones emphasizes its importance. Secondary reflexes undoubtedly not only provoke the after-effect in the individual reflex, but to a great extent

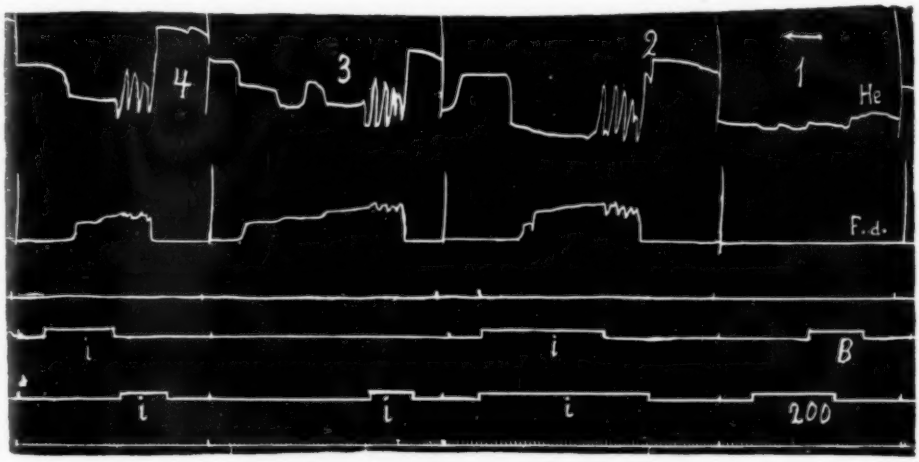

FIG. 7.

Fig. 7. "Bob," November 20, 1917.—The relation of the individual reflex excited by a sound of 200 vibrations per second to the unusual sound of a bell. In the first experiment the bell was rung before the sound of 200 vibrations, and the latter produced no reflex of the limb (bottom curve), or of the head (top curve). In the second experiment the bell was rung for 26 seconds during the sound, and the reflex ceased 17 seconds after it started. In the third experiment the reflex was produced without the bell; the after-effect lasted 27 seconds. In the fourth experiment the bell was rung during the period of the after-effect, and 8 seconds after the starting of the bell the after-effect ceased.

favour and reinforce the primary reflex to an individual stimulus. But we must also bear in mind that the secondary reflex may arise not only in response to secondary stimuli, but in immediate response to the

primary stimulus, for, as has been pointed out, the focus of the latter forms temporary connections with the foci of the secondary stimuli in the motor analyser.

Neither a primary individual stimulus nor a primary individual reflex is required for the formation of secondary temporary connections with the motor apparatus of the cortex, nor for their activity. Secondary reflexes can be formed under the influence of repeated electrical stimuli alone. At the beginning of my experiments on "Moura" I tried to form a reflex to a sound of 310 vibrations per second in combination with a thrice-repeated electrical stimulus. Such a combination was applied at intervals of 20 to 30 minutes.

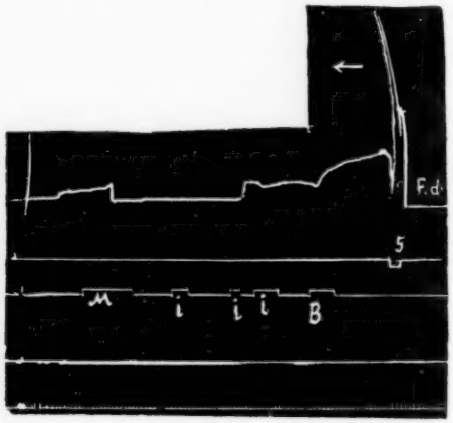

FIG. 8.

Fig. 8. "Bob," November 20, 1917.—The relation of the after-effect of a reflex elicited by an electrical stimulus to an unusual stimulus, such as a bell. First a short electrical stimulus was applied, which evoked a movement with a long-lasting after-effect. During the after-effect the bell was rung three times; in the first two instances it produced only a slight relaxation, the third time it completely stopped it. A little later the bell produced no movement, but the metronome, which was in this case the individual stimulus, evoked the usual effect.

In the course of the day three to five such combinations were made, in each of which the electrical stimulus lasted 1 to 3 seconds and was repeated every 3 to 5 seconds. Under these conditions the individual reflex to secondary muscular and articular stimuli developed long before

the formation of a primary reflex to the sound. Electrical stimuli began to produce a reflex with a persisting after-effect on the second day of the experiment, when the sound of 310 vibrations evoked no external reaction, not even an orientational movement of the head. The latter was evoked for the first time to a sound on the third day of the experiment (fig. 9).

As a result of the analysis of numerous observations it must be admitted that the composition of the cortical section of the arc of the

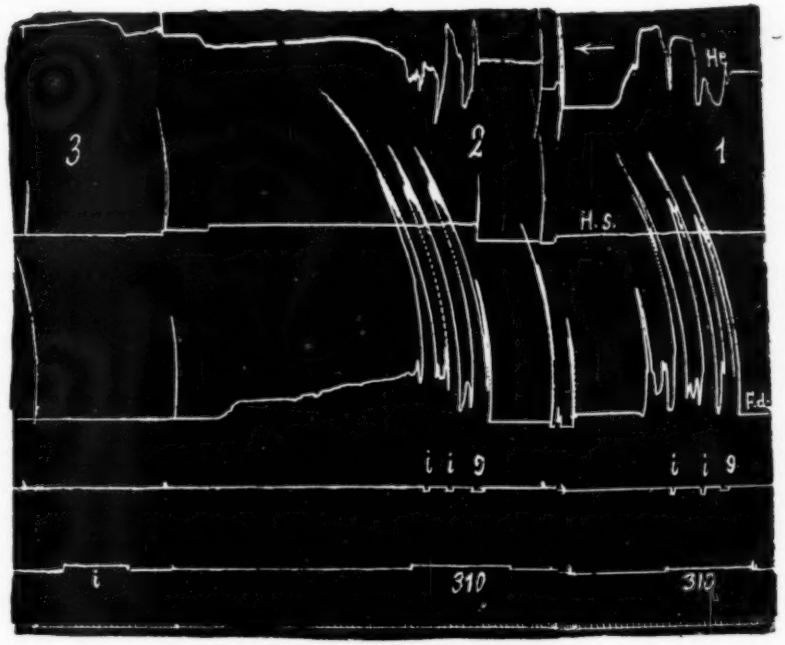

FIG. 9.

Fig. 9. "Moura" July 24, 1917.—The second day of work at the formation of a reflex of the right forelimb to a sound of 310 vibrations per second. The sound was combined with a thrice-repeated electrical stimulus, with intervals of 20 to 30 minutes between the combinations. The first record shows the fourth combination, and the second record the seventh. The third record shows the effect of the individual sound alone after the seventh combination. In the first experiment there is no after-effect to the electrical stimulus, but in the second experiment there is a long after-effect. The sound itself evoked no response in the third experiment.

individual reflex is very complex. The initial cortical point that receives the primary individual stimulus, in this case the sound, must be united with the final point, which represents the motor area of a certain limb, by four temporary paths of a different complexity, as is seen on fig. 10. One path is direct, being composed of a single connection from the initial point to the final one (D.N.); the second path includes two connections, the one extends from the initial point to the

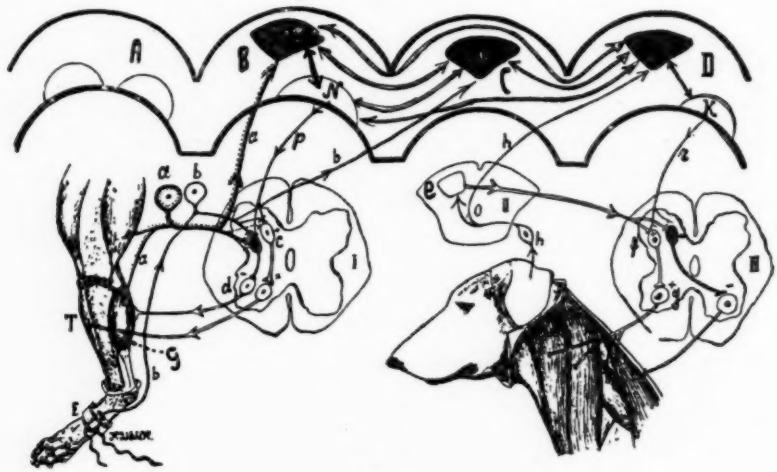

FIG. 10.

Fig. 10.—A rough diagram of the arc of the individual motor reflex to a sound in dogs. (B) The motor analyser in the cortex. (C) The cutaneous analyser. (D) The auditory analyser. (N) The cortical motor apparatus of the hindlimb. (K) The cortical motor apparatus of the neck. (I) The lumbar portion of the spinal cord. (II) The mid-brain. (III) The cervical portion of the spinal cord. (E) The stimulated part of the hindlimb with the electrodes placed over it. (a) The afferent path from the muscles of the hindlimb. (b) The afferent path from the skin of the hindlimb. (c) The co-ordinating apparatus of the flexion reflex. (d) The motor neurons of the antagonistic muscles of the leg. (e) The mechanism of orientational reactions in the mid-brain. (f) The co-ordinating apparatus for the movements of the neck. (g) The motor neurons of the neck muscles. (h) The afferent path from the auditory organ. The arrows indicate the paths between these sections and the direction of excitations in those connections on stimulation of the auditory organ by a sound, and on stimulation of the skin of the hindlimb. The double line arrows within the analyser denote temporary connections. p and r indicate the pyramidal tracts.

focus in the cutaneous analyser, the other from the latter to the final point (D.C.N.). The third path is also composed of two connections, one between the initial point and the motor analyser, the other between the latter and the final point (D.B.N.). The fourth path—the longest one—is composed of three connections, the first extending from the initial point to the cutaneous analyser, the second from this analyser to the motor analyser, and the third from the latter to the final point (D.C.B.N.).

The individual reflex is not, however, limited to isolated flexion of the limb; it is usually accompanied by an orientational reaction of the head, and sometimes also by a vocal reaction and by movements of other limbs, or even of the whole body. All these movements require the existence of numerous temporary connections. Even if the individual movement of the limb were accompanied only by rotation of the head, we would have to double the number of temporary paths, since the motor apparatus of the neck, and the part of the cutaneous analyser that receives secondary impulses from the joints, muscles and tendons of the neck would also participate in it. The number of temporary connections increases with the participation of new reciprocally acting points.

III.—On the Functions of the Cutaneous Analyser, the Motor Analyser and the Motor Apparatus of the Individual Reflex.

The temporary connection of the primary motor reflex of a limb develops between the analyser that receives the individual stimulus on the one hand and the cutaneous analyser, the motor analyser and the motor apparatus, on the other hand. In the secondary reflex it is formed between the motor analyser that receives secondary stimuli, on the one hand, and that same cutaneous analyser and the same motor apparatus, on the other hand. The question now arises: what are the special functions of the cutaneous analyser, of the motor analyser and of the motor apparatus in these individual reflexes? In this question two problems are involved: (1) Is it possible to define the part played by each of these parts, the temporary paths? (2) Can one of these parts function without the other?

The participation of the cutaneous analyser of the cortex in the individual reflex may be defined by the sum of the external effects. The first individual reflex is always and in all the dogs more or less violent, and accompanied by the usual signs of displeasure, as groans and move-

ments of the head; in some dogs these are the first signs of the individual reflex. This mode of expressing displeasure at the individual stimulus diminishes in course of time, and reappears only under certain conditions. Now, the individual stimulus usually provokes only an isolated flexion, with a slight orientational reaction of the head. This change in the individual reaction in the course of development of the temporary connections shows that some which played an essential rôle at first cease to participate in the reflex later. The violent reactions evoked at first by the individual stimulus depend upon the activity of temporary connections, including the cutaneous analyser. When other paths develop, the activity of these diminishes.

The temporary connection must first of all develop through the cutaneous analyser. Electrical stimulation excites the cutaneous analyser first and most strongly; therefore its reciprocal action on the focus of the individual stimulus must develop early. The motor apparatus of the limbs and of the other organs is already excited from the cutaneous analyser owing to irradiation, though in a less intense form. That is why temporary connections with the former apparatus develop later. But, as it has been pointed out in the first article, the same electrical stimulus that at first provokes a violent reaction and an expression of pain, later evokes an isolated flexion of the limb without any expression of discomfort. Such a change in the cortical reaction indicates that, in the course of time, the connections between the focus of the electrical stimulus and the motor apparatus of the stimulated limb acquires greater importance. This is conditioned by the existence of closer anatomical and functional connections between the cutaneous analyser and the motor apparatus of the limb; consequently the excitability of the latter is raised the more. This fact influences strongly the special development of an immediate connection between the focus of the individual stimulus and the motor apparatus of the stimulated limb. As a matter of fact, on the development of the simplest temporary path the more complex paths connected with the cutaneous analyser do not disappear entirely. Their activity may be seen in certain conditions that raise the excitability of this analyser and of its temporary connections. The excitability of the cutaneous analyser, for instance, may be raised by a weak electrical stimulus that evokes neither groans nor other movements indicating displeasure. But if the individual sound is tested soon after such a stimulus, it may evoke loud groans and a violent reaction of the head and limbs, instead of the usual isolated flexion of the limb (fig. 11). This violent individual

reflex may continue for a long time if the preceding electrical stimuli had provoked a strong effect, as howling. It does not matter whether this stimulus is applied in combination with an individual stimulus or alone, nor to which limb it is applied.

When the experiments have been interrupted for one or two days the first sound seldom evokes a violent reflex, but this may occur after an electrical stimulus, and when the excitability of the animal is high. It was generally noticed that the greater the excitability of the animal,

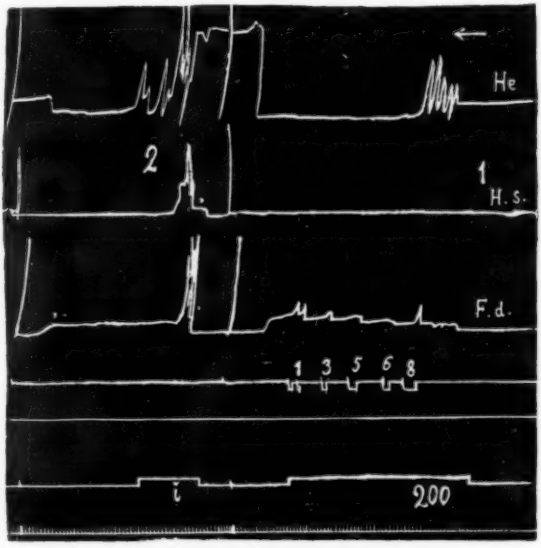

FIG. 11.

Fig. 11. "Bob," February 18, 1917.—The influence of a preceding combination with an electrical stimulus on the individual reflex. In the first experiment the usual reflex of the right forelimb to a sound of 200 vibrations per second was combined with an electrical stimulus which provoked only a feeble augmentation of the existing individual reflex. In the second experiment, made five minutes later, a repeated individual sound evoked a series of rapid movements of the limbs and head, with persistent flexion of the right forelimb.

the more marked was the violent stage of the movements. All these facts convince me that the violent part of the reaction depends on the cutaneous analyser. Preceding electrical stimuli favour the violent

reaction since they raise the excitability of the cutaneous analyser. In the same way the appearance of a violent reaction on a general rising of excitability depends upon its increased excitability.

The duration of the violent stage of the individual reflex does not depend on the duration of the sound ; it matters not whether this lasts one or several seconds. This shows that the main effect of the sound is to excite the activity of the cutaneous analyser. The duration of the reflex depends on the functional state of the latter, and on secondary stimuli of muscular and articular origin. We have already seen that the latter are, in fact, capable of eliciting violent reactions. It is consequently necessary to assume that the general or violent part of the individual reflex, associated with expressions of discomfort, is probably conditioned by the activity of the cutaneous analyser.

This deduction allows us to conclude that an isolated flexion of the limb after general movements, or apart from them, generally occurs without the participation of the cutaneous analyser, chiefly owing to the temporary connections that develop between the analyser that receives the individual stimulus and the motor apparatus of the limb. The persistence of the reflex after the cessation of the sound must also be conditioned by the activity of secondary temporary connections between the motor analyser which is affected by secondary stimuli and the motor apparatus.

During the stage of generalization of the reflex, when excitability is considerably raised, violent reactions may occur in response to unusual stimuli. For this the participation of the secondary temporary connections is not necessary, for the reactions may depend on the cutaneous analyser, the activity of which may be evoked by a general irradiation of the excitation initiated by the unusual stimulus.

The law of "interdependent" radiation explains the diminished activity of the temporary paths of the cutaneous analyser when the reflex is fully differentiated to unusual stimuli, and is localized in its peripheral manifestations. These temporary paths are very complex, and consequently in them the excitation meets less favourable conditions for spreading from the initial point to the motor apparatus than in simple paths that do not include a cutaneous analyser. The greater the number of stations through which the impulse has to spread the more it diminishes in intensity. The reciprocity between the initial and the final points of the temporary paths is greater, the simpler the path and the fewer synapses it contains. The simplest temporary path is one that connects the initial point directly with the

final one by means of one temporary connection; it is therefore more highly developed than other paths. This explains the fact that, according to the law of "interdependent" irradiation, the excitation irradiates to a less extent from the initial point along complex paths that include a cutaneous analyser, especially when the excitability of the latter is not much increased by electrical or other stimuli.

The participation of temporary paths which include a cutaneous analyser may be detected in every reflex by the external manifestations. These always appear in the form of general movements of the whole body and groans. These paths are very active at the beginning of the formation of the reflex, but later, on the development and organization of more simple temporary paths which do not include a cutaneous analyser, this activity diminishes, owing to the predominant spread of the excitations along simple paths, according to the law of "interdependent" irradiation.

IV.—Conclusions.

The analysis of these observations leads us to the following conclusions with regard to the functional elements included in the arcs of individual reflexes.

(1) The cortical part of the reflex arc of an individual motor reflex of a limb is composed of: (*a*) a part of the analyser that receives the individual stimulus; (*b*) a part of the cutaneous analyser that is excited by the electrical stimuli; (*c*) the motor analyser which receives secondary (proprioceptive) stimuli of muscular and articular origin; (*d*) the motor apparatuses of the cortex that are in close innate connection with the motor analyser, and finally (*e*) numerous temporary connections between these elements of the cortex, constituting temporary paths of various complexity.

(2) Numerous secondary reflexes are superadded to the primary individual reflex excited by an individual stimulus, owing to the establishment of special temporary connections between the cutaneous analyser and motor apparatus excited in the primary reflex, and the part of the motor analyser excited by secondary (proprioceptive) stimuli from the tendons, muscles and joints. The persistence of the reflex after the cessation of the individual stimulus is conditioned chiefly by the activity of these connections.

(3) In primary as well as in secondary reflexes the activity of complex temporary paths with a cutaneous analyser is shown by general movements and vocal reactions, while the activity of simple

temporary paths without a cutaneous analyser manifests itself by isolated movements of the limb.

(4) On the strengthening of the individual reflex the complex temporary paths of both primary and secondary reflexes become less excitable and active, owing to the greater development of temporary connections in the simple than in the complex paths.

(5) The formation of temporary connections is a function of the cortex of the cerebral hemispheres; they are formed exclusively between elements of the cortex, and never between cortical and subcortical elements. All connections between cortical and subcortical elements are innate.

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Proceedings of the Section of Neurology of the Royal Society of Medicine.

Dr. WILFRED HARRIS in the Chair.

Meeting held April 10, 1924.

Discussion on the Value of X-rays in the Localization of Cerebral and Spinal Tumours, with special reference to Ventriculography and Lipiodol Injections.

MR. PERCY SARGENT said that during a recent visit to Professor J. A. Sicard's clinic in Paris he had been greatly impressed with the possibilities of Sicard's method of investigating spinal lesions by means of radiography after injecting into the spinal theca a substance opaque to X-rays. The fluid used is "lipiodol," a thick inert oil containing 40 per cent. of iodine. No bad effects had been noted from the presence of so strong a solution of iodine, probably owing to the fact that the oil parts with the iodine with extreme slowness. In one case lipiodol injected into the muscles of the back could be clearly seen by means of the X-rays two years afterwards.

The technique was then described. With the patient sitting up in a chair, an ordinary lumbar puncture needle is introduced in the mid-line between the atlas and the occipital bone. As soon as the atlanto-occipital ligament is pierced, a little cerebro-spinal fluid is withdrawn and 1 or 2 c.c. of the lipiodol are injected. When no block exists the lipiodol falls very quickly to the bottom of the theca, and can be seen by means of the X-rays as a cone-shaped mass opposite the second sacral vertebra. When a complete block is present the whole of the lipiodol is arrested, and indicates clearly the relation of the point of blockage to the bones. The lower limit of the block can be ascertained by injecting, at a second sitting, some more lipiodol through a lumbar puncture, and taking a radiogram with the patient head-down. As extramedullary tumours are usually small and intramedullary tumours often extend over many segments, the method may prove to be of value in distinguishing between those two kinds of spinal tumour. It is also useful to indicate a level for operation when the exact segmental site of a lesion is not clearly shown by the neurological signs. It has also been employed in cases of fracture of the spine as an aid in determining whether a gross extramedullary lesion exists such as might be relieved by operation. From the surgical standpoint the method in cases of tumour gives the exact relation of the tumour to the bones,

so that it can be approached with greater precision and through a smaller wound.

Mr. JEFFERSON proposed to run over various points in the Röntgen diagnosis of cerebral tumours so far as he could to illustrate them from personal cases.

The matter may well be divided under three headings: first, the general changes in the skull brought about by increased intracranial tension; second, the local changes in the bone produced by tumours in their immediate vicinity; and third, the somewhat different category of ventriculography.

The general changes in the skull.—General changes are naturally most marked in those cases where obstruction to the cerebro-spinal pathway has resulted in ventricular back-pressure and dilatation. These changes may show themselves on the X-ray plate in the following forms:—

(1) Sutural diastasis: The extent of the opening up of the suture lines is a very variable quantity. It is well seen in children up to the age of 10 or 15 years, and I have noted it in a young man 23 years of age. I cannot say at what age it may no longer be expected, but I have not noted it usually in adults. It is most marked at the coronal suture. In the ordinary lateral view it may be seen as a definite widening or sometimes as an ill-defined white streak upon the film or plate. The widening of the sagittal suture is usually at least as well marked, but for technical reasons it is difficult to detect. Sutural diastasis will most commonly be found in cerebellar tumours in young people, or in obstructive hydrocephalus of adhesive origin. From the practical point of view the periodic X-ray examination of a hydrocephalic skull may be of some value. For, in general, separation of the suture is only seen in a pronounced form in acute or progressive cases. The powers of bone growth along the suture lines is so great that the bone defect tends rapidly to be repaired. When a balance has been struck, in those cases which I may, perhaps, term "compensated hydrocephalus," diastasis is no longer a feature of the X-ray photograph.

(2) Ribbing of the skull or convolutional atrophy. The peculiar and unmistakable ribbing of the skull, aptly likened to the ribbed sand seen on many seashores at low tide, is a characteristic feature of many X-rays of tumour subjects. It is usually localized to the anterior third of the skull, and for this reason has not won universal acceptance as a definite result of intracranial pressure increase. It is not an infallible sign, and in the absence of choked disc, and so forth, must be regarded as of no special importance. My own experience leads me to the conclusion that it is quite certainly a sign of increased pressure. A certain slight degree of convolutional marking is normal in the skull. In only one case of several hundred have I seen a high grade of ribbing in a case with normal pressure.

According to Hever and Dandy, and apparently according to Spiller, this patterning of the skull is due to atrophy of the inner table. With this view I cannot agree. It seems to me much more probable that it is due to diploetic compression by which the two tables tend to near one another at points corresponding with the convexities of the gyri.

(3) Sellar distortion. I shall not deal with pituitary growths themselves, as a sufficient literature on the radiographical appearances of these tumours exists and is widely known.

Sellar distortion is most frequently seen in patients with ventricular dilatation. The sella is normally in relationship with the floor of the third ventricle, and when hydrocephalus is present the floor of the third ventricle bulges to a considerable degree. The results of the fluid pressure are first an opening up of the diaphragma sellæ and often actual compression of the hypophysis. Later the pressure may lead to erosion of the dorsum sellæ and posterior clinoid processes, but this sequence is not invariable and will depend on certain anatomical facts. In the first place the relationship of the floor of the third ventricle to the dorsum sellæ is variable; in the second place the strength of the moulding of the sella is variable; and in the third place it is obvious that the hydraulic pressure must often be insufficient or not long enough continued to bring about erosion. That these mutable factors are important is shown by the fact that a large number of cerebral tumours and a certain number of hydrocephalics present no notable change in sellar contour. On the other hand, more than one surgeon has mistakenly operated upon the hypophysis on the evidence of sellar deformity and has tapped the floor of a dilated third ventricle instead of the pituitary cyst or tumour which he expected to find there.

Local changes in the bones.—Hyperostosis of the bones overlying an endothelial or meningeal tumour has won for itself a definite place in cerebral pathology. Whether or not this bone furring or thickening will be recognizable on an X-ray film will always be partly a matter of good fortune and partly a matter of good management. Only superlatively good pictures can be relied on to give us the evidence which we need. And in order that any help may be obtained in the recognition of basal growths stereoscopic views are necessary.

Unfortunately for us as clinicians, actual erosion of the cranial bones is apt to be more extensive on the base of the skull than over the upper surface of the hemispheres. The reason for this is twofold. First, because the bone of the floor of the skull is rather thinner; second, because the tumour tends to be tethered through the fixation of the membranes at the foramina in the base. That the latter is rather the more important of the two is shown by the fact that the dense bone of the petrous portion of the temporal may be destroyed by an endothelioma in the middle fossa which has been fixed by the branches of the trigeminal nerve and the normal adhesions of the membranes about the foramen lacerum.

Shadows cast by cerebral tumours themselves.—If we exclude the tumours of Rathke's pouch, calcification is an uncommon event, uncommon certainly when it is of such degree that opacities are found on X-ray examination. Personally, I have not seen a tumour shadow in my series. One may very easily mistake a patch of calcification in the clinoid plexuses, pineal or falx for a tumour shadow. I have come across two examples of these shadows accidentally, in patients who had been X-rayed for some other purpose. The true nature of

these opacities can generally easily be demonstrated by the antero-posterior view. The calcified areas will then be seen to be symmetrically placed on either side of the mid-line (if choroidal) or dead in the centre if the plaque is in the pineal gland or falx.

VENTRICULOGRAPHY.

We must now turn to a different subject, to air-replacement of cerebro-spinal fluid as a clinical aid to diagnosis. It is not an end in itself. It is useful in those cases where localization of tumours by neurological means is doubtful or impossible. Ventriculography has won for itself a definite place in diagnosis, but it is none the less still in an experimental stage. The reason for this is the technical difficulties which surround it, not only in actual performance but more particularly in interpretation. We must, I think, look forward to improvements; I should say that the chief improvement will probably come through the use of stereoscopic X-rays and of the Potter-Buckey diaphragm.

I have been disappointed with the results of injecting small quantities of air, 25 c.c. and less. This should be enough to give one a good picture of one ventricle, and here improvement in the X-ray technique will be most useful. Unfortunately the Americans who most enthusiastically support air replacement have left us sadly lacking on important details.

The chief objections to ventriculography are, first of all its risk, and secondly the fact that even when that risk is taken we have no guarantee that we are going to get anything very helpful from it. But these objections are I believe surmountable with practice and experience. There is no doubt that the method is one which is only justifiable in the hands of a neurological surgeon who is fully cognizant of the intracranial physiology, and who will be able to use the resources of his experience to counter unpleasant happenings when they arise.

My own experience to date includes thirteen injections on ten cases. One patient, a blind hydrocephalic child, died three days after the injection, but it was so advanced in disease that it might have died from natural causes. The other was a woman with an unlocalized tumour. I tried a double puncture of the posterior horns and failed to withdraw cerebro-spinal fluid for some reason unexplained. She died seven days later and a post-mortem examination was refused. I am inclined to use the method sparingly. The upholders of this method have harmed their cause by claiming too much for it, and by publishing photographs of tumours which should have been localized easily enough by less dangerous means. But if in ventriculography we have a method which may help us to decide that a tumour is not present (e.g., a posterior fossa arachnoiditis with secondary hydrocephalus, pseudo-tumour) or to localize it when the patient is blind or otherwise non-co-operative, then we must admit that we have added a new weapon to our armoury. The chief danger appears to me to be its too indiscriminate use, particularly by surgeons who have had no great experience or training in cerebral surgery.

Sir JAMES PURVES-STEWART recounted his experiences in the use of lipiodol and of ventriculography, and emphasized the important assistance both methods might be as an aid to clinical diagnosis. He showed a series of lantern slides illustrating the arrest of lipiodol by tumours and other compressing lesions of the spinal cord. In his experience the method is without danger and has no serious disadvantages, though in one case in which the injection was exceptionally difficult owing to the obesity of the patient, some of the lipiodol passed through the posterior cistern into the base of the brain where it produced a facial nerve palsy. This has, however, recovered.

It has been his custom to introduce air into the cerebral ventricles by lumbar puncture after withdrawing some of the cerebrospinal fluid rather than by trephining. In his opinion this method is safer and gives equally valuable results. He pointed out that there were many fallacies in the interpretation of the radiograms, and that, even under the most careful circumstances, they frequently failed to indicate the position of the tumour.

Mr. MCCONNELL used ventriculography in fifteen cases of cerebral tumour, and in ten of these he had obtained definite information as to the localization of the lesion. He had had two fatalities, one patient dying eight and the other fourteen hours after the injection ; in both the tumour lay in the posterior fossa of the skull. He believed the danger could be considerably reduced by varying the intracranial pressure as little as possible, by removing only a small amount of fluid, as 2 to 5 c.c. at a time, from the ventricles and immediately replacing it by a corresponding amount of air. In many cases he had had considerable reactions, probably owing to the increase in intracranial pressure. During the procedure the state of the blood-pressure is the most valuable indication of the condition of the intracranial pressure. He invariably introduced air through a small trephine opening made on Keen's point; he believed the results obtained by introducing air through a lumbar puncture are of much less value. He had found that the most useful information could be obtained by injecting one ventricle first, and after radiograms of it had been taken pumping air into the other ventricle. He recognized there are frequently difficulties in interpreting the results. The posterior horn is, for instance, frequently absent or cannot be distended, and consequently absence of air in it does not imply pressure in this region. In one case his needle struck a gliomatous cyst a few centimetres under the cortex of the brain and after withdrawing its contents he injected air into it. Radiograms which were then taken showed the extent of the cyst cavity and revealed a firm tumour projecting into it, which was afterwards removed by operation.

Dr. WILFRED HARRIS recognized the help both these methods might be in the localization of either a cerebral or spinal tumour. It seemed to him, however, that ventriculography was so dangerous that it should be employed on special cases only. Lipiodol injections in spinal disease gave some definite information and it seemed to him much less risky.

Dr. SIMMONDS referred to his experiences with lipiodol in three spinal cases. He described these three cases ; one of extramedullary tumour, one

of intramedullary tumour and one of meningitis, in which the use of lipiodol helped to determine the exact position of the lesion.

Mr. LANCELOT BROMLEY stated that in his experience lipiodol was particularly useful in defining the lower level. This, however, could not be ascertained accurately by clinical methods, and it is, of course, important for the surgeon to know how low the tumour or other compressing lesions may extend. He believed that a certain amount of valuable information could be obtained by knowing the rate at which the lipiodol fell. A tumour sufficiently large to produce a considerable degree of spinal compression usually blocked the theca completely, while in meningitis the lipiodol fell more slowly and drops of it were usually held up at different levels of the vertebral canal.

Dr. HILDRED CARLILL referred to the injection of lipiodol by high dorsal puncture rather than by cisternal puncture and he thought that in some cases it was preferable. He inquired if any accidents had occurred after its use.

Mr. PERCY SARGENT, in replying, said that he had seen no ill effects from the use of lipiodol, and was not aware that any fatalities had followed its employment. He was convinced that cisternal puncture was much safer than high dorsal puncture; the latter was, in his opinion, so dangerous that it could be justified only in exceptional cases. The rate at which the lipiodol falls is a difficult problem. In a case in which lipiodol had fallen slowly and left drops at different levels he suspected arachnoid adhesions, but this is not always so.

Mr. JEFFERSON said he recognized that ventriculography is still a dangerous procedure, though a smaller proportion of bad results had been obtained by more experienced surgeons. He added that if Sir James Purves-Stewart's method of injecting air by lumbar puncture has any advantage, they certainly excited very intense headache and severe reactions.

Sir JAMES PURVES STEWART condemned high dorsal puncture. He still maintained that the introduction of air by lumbar puncture is preferable to making a trephine opening in the head and then introducing air directly into the lateral ventricle, as air may be quickly absorbed after it has been introduced before it can be replaced by a correspondiug amount of cerebrospinal fluid. There were then liable to be dangerous variations in pressure. He thought this was probably the explanation of some of the fatalities which had occurred.

Mr. MCCONNELL doubted the advisability of introducing air by lumbar puncture, for no reliable results could be obtained unless we were quite certain of having the ventricles full of air.

Notices of Recent Publications.

Körperstellung: Experimentell-physiologische Untersuchungen über die einzelnen bei der Körperstellung in Tätigkeit tretenden Reflexe, über ihr Zusammenwirken und ihre Störungen. (Monographien aus dem Gesamtgebiet der Physiologie der Pflanzen und der Tiere.) By R. Magnus. S. 730, und 263 Textfiguren. Berlin: Springer. 1924.

In the preface to his book, Professor Magnus relates the fortuitous circumstance which first led him to make the investigations which form its subject matter, and which have added to the physiology of the nervous system one of the most fascinating chapters in its history. In the fifteen years which have elapsed since his original observation, Magnus and his collaborators, amongst whom he gives the place of honour to Dr. Kleijn, have recorded in a series of over thirty papers their experimental researches into the problems involved in the nervous regulation of posture. It is seldom that physiological literature has contained a more lucid and impressive account of ingenious experiment, of difficulties overcome and of exact knowledge gained. It must, moreover, be a source of considerable pride to the English school of physiology to realize that it is upon foundations so securely laid during the past thirty years by Sir Charles Sherrington that the masterly work of the Utrecht school has been built.

The researches of Sherrington, in which he has revealed the nature of muscle tone as a purposive reflex reaction and the basis of all postural activity on the part of the musculature, are now becoming so well embodied in clinical neurological thought that it is scarcely necessary to refer to them except in so far as is required to indicate the point at which the work of Magnus first arose.

The animal preparation so successfully employed by Sherrington in his investigations on muscle tone is the so-called "decerebrate preparation." This is an animal in which the brain-stem has been transected in the region of the tentorium. The limits between which such a transection must fall are now closely defined, the headward limit being the coronal plane of the posterior corpora quadrigemina, and the tailward limit the plane of entry of the eighth nerves. Following transection between these limits all the muscles which normally maintain the animal in its standing posture enter into a state of hypertonus. The adequate stimulus arises in proprioceptive nerve endings in the tonic muscles themselves, and it is within the last few months alone that Sherrington and Liddell (*Proc. Roy. Soc.*, B, 1924, 96, 212) have found that tension or "stretch" is the adequate stimulus, and have been able to describe

the conditions governing the development and incidence of the necessary tension. It follows, then, that the integrity of the muscular afferent nerve supply is a fundamental condition of the development and maintenance of tone.

During the spring of 1909, as he relates, Magnus chanced to be working with a decerebrate preparation, and noticed when he turned the animal from the lateral into the supine position that the extensor tone of its limbs underwent an appreciable increase. Further, when the animal's head was flexed upon the trunk so that the line of the mouth made an angle of 45 degrees above the horizontal, a further increase was observed to occur after a latent period of several seconds. These modifications of tone persisted as long as the new position of the head which evoked them was maintained.

At the same time and independently, Sherrington was making similar observations. Thus, he noticed that when the animal's head was rotated, the limbs on the side to which the vertex was turned showed an inhibition of their extensor tonus. Extirpation of the labyrinths did not abolish the phenomenon, which disappeared when the upper cervical posterior roots were divided. The reaction was therefore a reflex arising in nerve endings in the deep structures of the neck (*Journ. Physiol.*, 1910, 40, 28).

These observations formed the starting point of the work described in detail in the book under consideration, and have resulted in the discovery and classification of an extremely complex series of reflex reactions of proprioceptive origin, of which variations in muscle tone, and therefore of attitude, are the expression. The otolith organs of the labyrinths (and not the semicircular canals) and proprioceptive nerve endings in muscles, tendons and joints throughout wide regions of the body are the sources of the reactions, which constitute the mechanism by which the animal maintains the various postures taken up during the course of its multifarious motor activities. In addition, a series of reflex movements, phasic reflexes, arising from stimulation of the semicircular canals, have been observed, and these together with the tonic reactions referred to underlie the capacity of the intact animal to maintain its equilibrium as it moves through space.

In short the combined researches of Sherrington and Magnus and their co-workers have elucidated the nature of the motor activities of the cord, brain-stem and cerebral cortex, and have made possible for the first time a scientific analysis of the numerous and baffling disorders of movement which, occurring in the course of disease of the nervous system in man, have provided clinical neurologists with problems which are in many instances still extremely obscure.

Beginning their investigations, for reasons which will be apparent later, with the decerebrate animal, Magnus and De Kleijn found that by imposing passive variations in the position of the animal's head in relation to space and in relation to its body certain constant modifications of tone in the muscles engaged in reflex decerebrate rigidity could be produced. These variations were expressed by changes of limb posture as well as by palpable modifications of the decerebrate rigidity.

Two main groups of reactions were differentiated, tonic labyrinthine and tonic neck reflexes. In each instance the reaction is tonic in the sense that it is produced not by the movement of the head, but by the new position imposed upon it, and that it persists as long as this is maintained. Its latency is characteristically long, amounting in some instances to several seconds, a feature in which it differs remarkably from reflex movements elicited by cutaneous stimulation.

It is the otolith organ of the labyrinth which is involved, the adequate stimulus being a variation in the relation of the maculæ of the utricle and saccule to the horizontal plane of space. The maximal reinforcing influence of the labyrinths upon extensor tonus is developed when the otoliths depend from, the minimal when they rest upon, the maculæ.

Taking the animal as a whole, labyrinthine influence is maximal when the animal is in the supine position and the line of the mouth makes an angle of 45° above the horizontal, and minimal with the animal in the standing position and the line of the mouth at an angle of 45° below the horizontal. Intermediate grades of extensor rigidity are observed in intermediate positions of the animal according to the degree in which these approximate to the maximal and minimal positions respectively.

These positions have been found to be approximately the same for all animals from the guinea-pig to man. The extensor tonus of all four limbs is identically influenced by the tonic labyrinthine reflexes.

After bilateral destruction of the labyrinths, modification of extensor tonus in the limbs may still be produced by varying the position of the head, but now the variation must be in relation to the neck and trunk. The tonic neck reflexes, for so the reactions in question are called, arise in proprioceptive nerve endings in the deep skeletal structures of the neck and they are abolished by bilateral section of the upper cervical posterior roots. They may be investigated free from complication after bilateral labyrinth extirpation. Rotation ("Drehung") of the head on the long axis (snout-foramen magnum), lateral flexion ("Wendung"), dorsal and ventral flexion, all produce characteristic tonic responses in the limb musculature. Thus, rotation to the right (that is in the rabbit, vertex to right, snout to left) is followed after a delay of one or more seconds by increased extensor rigidity in the left limbs ("Kieferbeine") and by diminished extensor tone in the right limbs ("Schädelbeine"). Lateral flexion to the right produces increased extensor tone in the right limbs, diminished in the left. When rotation and lateral flexion are combined they antagonize in their results, but the former being the more potent stimulus, its effect predominates. Dorsal flexion reinforces extensor tonus in all limbs in the rabbit, but effects the fore and hind limbs reciprocally in the cat, increasing extensor tone in the former, inhibiting it in the latter. Ventral flexion has the reverse effect to dorsal flexion.

It is comparatively easy to demonstrate these reactions in the normal cat. If a piece of meat be held before the standing animal at a level higher than the head, the fore-limbs stiffen in extension, while the hind-quarters sink down on

the flexed hind-limbs. If it be placed on the floor before the animal, the fore-part of the animal sinks on the flexed fore-limbs, the hind-limbs remaining extended and supporting the hind-quarters in the initial posture.

It is clear that in the different positions of the animal in space, the tonic labyrinthine and neck reflexes, when both are active, combine variously. This, and the fact that while in some animals the former are the more intense and in others the latter, renders the analysis of the numerous reactions a matter of some difficulty. Moreover, since certain labyrinthine reflexes act upon the neck musculature, and this more intensely than upon that of the limbs, it follows that the changed position of the neck thus produced gives rise in turn to secondary neck reflexes acting upon the limbs. When two or more tonic reflexes act simultaneously upon a given muscular territory they tend to sum algebraically, in the manner that Sherrington has described in connection with double reciprocal innervation.

In addition to the reactions described, the position of the eyes is also influenced by variations in head posture and for each given posture of the head there is a corresponding position of the eyes ("Kompensatorische Augenstellungen"). It is in animals with laterally placed eyes and without binocular vision that tonic labyrinthine and neck reflexes acting upon the eyes are best developed. In animals with frontally placed eyes and binocular vision, the adjustment of the eyes to variations in the position of the head is affected by means of retinal stimuli.

The tonic reactions we have been considering constitute the total of such postural reflexes obtainable in the decerebrate animal, and the predominance of the head as determining body posture is very clear. It is equally certain, however, that such an animal preparation has no power of reflex control over the position of the head in space or in relation to the trunk. It is only by imposing variations in head posture that the reactions in question can be elicited, and they are capable of no more than maintaining the animal in such attitude as may be imposed upon it in this way. The animal can stand, but it cannot change its posture without outside interference. If it be thrown on to its side, it lies there motionless in the position determined by gravity, and when erect its standing is a passively imposed condition. Moreover, the attitude is not quite that of the intact animal; it is, in Magnus's phrase, a caricature of standing. The sum total of the tonic reflexes so far considered, Magnus groups as "standing reflexes" ("Stehreflexe"), and it is clear that in the intact animal there must be other reactions which allow of the righting of the head in space, and thus of adjusting the body to a variety of postures. These additional reflexes are known as "righting reflexes" ("Stellreflexe") and they are present when brain-stem transection passes headward of the limits we have named earlier. An animal so treated is known as a "thalamus animal" when transection passes headward of this structure, and as a "mid-brain animal" when transection severs the cerebral hemispheres including the thalami. The essential condition in either case, from the point of view under consideration, is that the whole

of the mid-brain shall be left in the continuity with the pons, medulla and cord.

Although deprived of the cerebral hemispheres, the mid-brain animal is seen at once to differ profoundly from the so-called "decerebrate animal." After the operation is complete the anæsthetized animal is laid upon its side. As it emerges from anæsthesia, it raises its head, the forepart of the trunk follows, then the hind part, and finally the animal assumes a squatting position. The distribution and intensity of muscle tone is normal throughout, and there is no rigidity. Such an animal is an automaton deprived of all volition, and whatever activity it shows is purely reflex. All the normal nutritional reflexes and many pseudo-affective reflexes are present. It jumps when a loud noise is made in its neighbourhood. If such an animal be laid upon its side or back, it rights itself at once. Under appropriate stimulation it can step, run and jump with perfect co-ordination, and when its movements cease it resumes the sitting posture. In whatever position the animal be placed, the head at once rights itself, and the animal clearly is in possession of reflex reactions which keep the head always right side up in the world, and since the position of the head governs that of the trunk and limbs it has reflex control over all its postures. The following groups of "righting reflexes" (for so Magnus favours the anglicizing of "Stellreflexe") have been analysed. (1) Labyrinthine reflexes acting upon the head; (2) reflexes arising in the body wall and acting upon the head; (3) reflexes arising in the neck secondary to (1); (4) reflexes arising in and acting upon trunk and limb musculature; and (5) in the intact animal a fifth group of righting reflexes arising in the retinæ. When the labyrinths are both destroyed and the animal is blindfolded, it loses the capacity of righting the head in space. When vision is free it is able to do so, even after bilateral labyrinth extirpation. Optic righting reflexes are present in cat, dog and monkey, but not in the guinea-pig or rabbit.

All the reactions so far considered are purely reflexes of position ("Statische-reflexe," "Reflexe der Lage"), and in so far as they are labyrinthine in origin, they arise in the otolith organs of the utricle and saccule. They are not due to currents of endolymph in the semicircular canals, stimuli which give rise, as we shall see, to reflexes reactions of quite another kind. If a guinea-pig be centrifugalized and the otoliths thus thrown down and rendered inactive, all tonic labyrinthine reflexes are abolished, but semicircular canal reflexes persist. By such means, the two varieties of labyrinthine reflex may be studied separately, and not the least of the fruits of Magnus's work has been to show that functionally the labyrinth is a dual organ. In respect of the central nervous mechanism of the tonic reflexes, the important point has been established that the grey matter of the arcs concerned lies entirely within the brain-stem, mid-brain, pons and medulla, and the afferent and efferent limbs of the arcs in no case traverse the cerebellum. Extirpation of this structure does not abolish a single member of the series of tonic reactions we have been considering. Recent investigations by Rademaker, carried out in Magnus's laboratories and at his inspiration, have shown that the "centre" for the righting reflexes is

situated in the red nucleus, and a detailed account of these investigations is included in the book.

Of equal interest and importance is the group of so-called "stato-kinetic reflexes" studied by Magnus and his school. Unlike the tonic reflexes, these are evoked not by changes of head, trunk or limb posture, but by movement, or more precisely by the initiation, cessation or variation of movement. Both rotation and movement in a straight line are effective under these conditions.

Rotation reactions.—If a sitting animal be rotated so that its head is at the periphery and its hind-end at the centre of the circle, and rotation be carried out to the right, then the head turns to the left (lateral flexion). On cessation of movement, the head turns to the right ("Kopfdrehnachreaktion"). Accompanying the head deviation is a head nystagmus and an after-nystagmus. In this the rapid component of the head movement is in the direction opposite to that of rotation, becoming reversed when movement ceases. The eyes show deviation of the same order as the head on rotation. In the case of the trunk and limbs, also, similar phenomena are seen, and Barany's pointing test after rotation is an example familiar to all clinical observers.

Reactions to movement in a straight line ("Reaktionen auf Progressivbewegungen") are also readily demonstrable in the intact animal. The animal is placed upon a horizontal board. If this be now moved vertically upwards, the animal sinks on flexing limbs. On cessation of movement the limbs extend. These movements take place at the beginning and end of movement respectively, and are spoken of as the "Liftreaktion." A similar phenomenon is seen when a guinea-pig is held vertically with the head downwards. If the animal be suddenly lowered, the fore-limbs spread out forwards as though to receive the weight of the falling body when the ground is reached ("Sprungbereitschaft"). Reactions of the same order arise in other regions of the body than the labyrinths, so that movement of one portion evokes movements in remote parts. The faculty by which a cat thrown or falling from a height always lands on its feet depends upon the combination of the various reactions we have been considering, both static and stato-kinetic. Labyrinthine righting reflexes bring the head right side up, and tonic reflexes secondary to these bring the trunk and limbs into line with the head. Reactions to progressive movement follow so that the animal alights nimbly on its feet.

In the course of their investigations, Magnus and de Kleijn have had occasion to study the effects of unilateral extirpation of the labyrinth. Armed with an exact knowledge of normal labyrinthine function they have had little difficulty in determining and analysing the disorders of function resulting from this lesion. In so doing they have provided a lesson not without significance for us as clinical neurologists. The analysis of disorders of function produced by disease of the nervous system has always exercised a considerable fascination over neurologists in this country, but it has not always been realized that a sound knowledge of normal function must precede any fruitful attempt in this direction.

After destruction of one labyrinth in the rabbit, the immediate results are

skew deviation of the eyes, nystagmus, rotation and lateral flexion of the head to the side of the lesion, some spiral rotation of the neck and trunk to the side of the lesion, increase of extensor tonus in the limb musculature on the normal, and diminution on the side of the lesion, and, in some instances, rolling movements. These symptoms may be divided into transient and permanent groups. The former include nystagmus and rolling movements, the latter include rotation of the head and neck, reciprocal alterations of limb tonus and deviation of the eyes. Skew deviation is characteristic of the rabbit and of animals with laterally placed eyes. In the cat and dog "skew" is minimal or absent. The nystagmus has a quick component to the mid-line, with a slow return to the side of the lesion. Head rotation tends to increase in degree for several weeks after operation and persists indefinitely. Spiral rotation of neck and trunk varies in intensity in different animals and tends to diminish progressively. Reciprocal tone changes in the limbs are permanent.

Analysis shows that the permanent symptoms may be divided into direct and indirect. The former are due to the unantagonized, or unbalanced, action of the intact labyrinth, and comprise head rotation and eye deviation. The indirect symptoms are due to head rotation, which sets up secondary tonic neck reflexes. These in turn cause the reciprocal tone changes in the limbs and the spiral rotation of the trunk. Directly, the labyrinths have but a transient effect upon limb tonus. The rolling is a forced movement, and is found to be due to running or leaping movements in an animal whose body is spirally rotated, so that when the forelimbs are vertical to the horizontal plane, the hind quarters and limbs are obliquely placed. Hence the animal progresses with a screw-like motion, and makes a complete rotation on its long axis to each two leaps. The movements occur in "attacks," and are attributed to stimulation arising in the fresh operation wound, and probably involving the central stump of the eighth nerve. Hence, rolling movements are in part "dynamic" in origin (in Luciani's phraseology) and in part of the nature of "release" symptoms. Magnus concludes that the labyrinth influences muscle tone in the limbs of both sides, equally that in eye and trunk muscles bilaterally, but predominantly on the crossed side, and the neck muscles on one side only; but in this instance the unilaterality is functional rather than anatomical, since muscles of both sides act in all movements.

The reactions to movement are semicircular canal reflexes, and, like the otolith organ reflexes already discussed, possess arcs which do not traverse the cerebellum.

Apart from the general interest which experimental researches must have for us, the book contains clinical observations in which the main tonic and stato-kinetic reflexes described in the animal have also been identified in man. Within the past four years numerous clinical applications of Magnus's work have been published, and have established fresh links between the physiology of the lower animals and man. It is to experimental work of the kind that clinical workers will now turn in increasing numbers for inspiration now that the possibilities of morbid histology have been fully probed.

We have already referred to the extreme lucidity of Magnus's exposition, and it remains but to note with admiration the excellent series of stereoscopic photographs with which the book is illustrated. It numbers over 700 pages and contains a wealth of minute experimental detail, but nevertheless its reading is a pleasure and the reader is nowhere lost in minutiæ.

With this brief and necessarily inadequate résumé of the contents of Magnus's book we have said enough to indicate the fundamental importance of the work which he and his disciples have carried out during the past fifteen years. The general principles governing the activity of the nervous system have been stated by Sherrington in "The Integrative Action of the Nervous System," a book which will always mark an epoch in the progress of our knowledge of the physiology of the nervous system. Magnus's book is one of the first-fruits of the application of this fundamental knowledge to specific problems of brain function, and it clears the ground for fresh additions to our knowledge, the scope and extent of which cannot yet be foreseen. A single example will make this clear. For forty years, since Luciani's first work on cerebellar functions was published, experimental physiologists and clinical neurologists have laboured in vain to define the functions of this organ and to analyse the results of its destruction upon the motor activities of the organism. We know now for the first time that a large number of so-called cerebellar defect symptoms are not primarily cerebellar in origin, but arise from associated labyrinthine lesions. In addition, the motor functions of the brain-stem and cord have at last been clearly described and defined, and the ground is now cleared for an attack upon the problem of cerebellar physiology. Sherrington and Magnus and their disciples have indicated the lines upon which such an attack must proceed, and, indeed, those upon which all similar investigations must be planned. We are, therefore, indebted to these masters of the experimental method, not alone for their rich contributions to exact knowledge, but also for their guidance as to the lines upon which future work may most hopefully proceed, and for the lessons of scientific imagination, precision and industry with which their work abounds.

F. M. R. WALSHE.

De Beteekenis der Roode Kernen en van het overige Mesencephalon voor Spiertonus, Lichaamshouding en Labyrinthaire Reflexen. (*The Significance of the Red Nuclei and the other parts of the Mesencephalon for Muscle Tonus, for Normal Attitudes and for Labyrinthine Reflexes.*) By Dr. G. G. J. RADEMAKER (from the Laboratory of Pharmacology at the University of Utrecht). Leiden: Eduard Ijdo. 1924.

The investigations recorded in this volume form, as it were, an anatomical supplement to the work of Magnus and de Kleijn, and as it has appeared in a language unfamiliar to most English readers it is necessary to give it a relatively full review which will at least indicate its scope and the main conclusions of the author.

The main aim of the volume has been to investigate the difference in behaviour between the thalamus-animal, that is one from which the forebrain and the corpora striata only have been removed, and the decerebrate animal.

The thalamus-animal preserves normal tonus in its muscles and can co-ordinate its movements; it is consequently able to stand, sit, walk and jump, and if it falls can regain its normal position immediately. It preserves all the "righting reflexes" of Magnus, except the optic righting reflex.

In the decerebrate animal, on the contrary, there is an abnormal hypertonus of the muscles, especially of the retractors of the head and neck, of the elevators of the tail and the extensors of the limbs. It can make walking movements, but cannot walk, and though its limbs may bear the weight of the body when it is placed on its feet, the animal cannot stand in a normal attitude. It falls on the slightest movement, and is unable to regain the standing posture. It has consequently lost all the "righting reflexes," except the neck-righting reflex which is initiated in the deeper structures of the neck and vertebral column, and maintains the body in the same relative position to the head.

In order to determine the levels of the nervous system in which the central mechanisms of these various reflexes lie transections were made at various levels of the thalamencephalon and of the mesencephalon in cats and rabbits. In the first place the author attempted to determine the most caudal level at which, after transection, the tonus of the muscles remained unaltered and the righting reflexes intact, and then the most oral level of transection below which extensor rigidity developed and the righting reflexes disappeared. These experiments proved that the normal tonus of the muscles persisted and the labyrinthine and body righting reflexes could still be elicited, after transection through a plane extending from the anterior part of the anterior corpora quadrigemina to the pes pedunculi, 2 mm. oral to the emergence of the oculo-motor nerves. Histological examinations showed that these sections always passed just oral to, or through the oral ends of, the red nuclei. On the contrary, extensor rigidity always developed and the righting reflexes disappeared after transection through a plane extending from the posterior part of the anterior corpora quadrigemina to the pes pedunculi, caudal to the emergence of the third nerves. This section passes through or just behind the caudal ends of the red nuclei. Section through the dorsal part only of the mesencephalon at this level does not produce decerebrate rigidity nor disturb the labyrinthine or body righting reflexes. The tonus of the muscles also remains normal, and these reflexes still persist after ablation of the whole of the dorsal part of the mesencephalon, including the corpora quadrigemina.

From these experiments it is concluded that the reflex centres lie in the ventral part of the midbrain between a frontal plane at the oral end of the red nuclei and the one immediately caudal to these. This conclusion is confirmed by the fact that transection of the ventral part of the mesencephalon at the more caudal level is always followed by rigidity and the loss of labyrinthine and body righting reflexes on the body.

In order to determine if the red nuclei play any part in the regulation of muscle tonus and in the labyrinthine and body righting reflexes, they were destroyed by small stab wounds in intact animals as well as after removal of the forebrain and in thalamus-animals. It was found that when rigidity developed and the righting reflexes disappeared Forel's decussation or the red nuclei were always injured, while these always escaped when the muscle tonus was normal and the righting reflexes unaffected. Similarly, after mesial sections between the anterior corpora quadrigemina the power of walking and jumping and of righting itself in response to labyrinthine and body stimuli were lost only when Forel's decussation was injured. In rabbits apparently it did not matter whether the forebrain had been removed or not, but in cats the rigidity was less extreme when the forebrain and the cortico-spinal tracts were intact. Similar results were obtained from stab wounds through the lateral aspect of the midbrain; when rigidity was present and the labyrinthine and the body righting reflexes were lost the wounds invariably injured the red nuclei, Forel's decussation or the rubro-spinal tracts, while these functions were always undisturbed when these parts escaped damage.

One very striking experiment was performed in a "thalamus rabbit." A fine silk thread was inserted through the middle line of the midbrain behind Forel's decussation. The animal could still walk and jump normally, but when the thread was drawn oralwards so that it injured Forel's decussation the animal at once fell, became rigid and lost its labyrinthine and body righting reflexes.

These experiments prove that the red nuclei and the rubro-spinal tracts are parts of the mechanisms for the maintenance of normal tonus in the muscles, for the labyrinthine righting reflexes and for the body righting reflexes on the body. Further, the red nuclei can still maintain these functions after removal of the forebrain, corpora striata, optic thalamus, the most oral part of the mesencephalon and the corpora quadrigemina. Magnus and de Kleijn have already shown that the red nuclei can regulate the labyrinthine righting reflexes after ablation of the cerebellum. Moreover, extensor rigidity develops when the red nuclei are injured, whether the forebrain and pyramidal tracts are intact or removed.

The author then attempts to correlate his experimental findings with many recorded clinical observations where disease in the midbrain, which probably or was actually proved to have damaged the red nuclei or their efferent tracts, was associated with muscular rigidity and disturbance of the "righting functions," and frequently with tremors or other involuntary movements. He therefore concludes that in man the red nuclei have similar functions to that which they possess in his experimental animals, that is, the cat and the rabbit. He also argues that the importance of disease of the cortico-spinal tracts, as a cause of hypertonus in man, has been over-estimated, and that it has not yet been proved that corpora striata or the substantia nigra possess the function of regulating muscle tonus.

In the later chapters of the book experiments are described which go to show:—

(1) That the centres for the body "righting reflexes" on the head lie in the mesencephalon at about the level of the red nuclei, but probably more dorsally;

(2) That the centres for the neck "righting reflexes" are situated caudal to the oral part of the pons;

(3) That the centres for the progression reactions (Liftreaktion—Springbereitschaft) also lie caudal to the oral end of the pons;

(4) That the rotatory head reactions and rotatory head nystagmus persist after ablation of the mesencephalon;

(5) That no centres oral to the oculo-motor nuclei are necessary for the various labyrinthine ocular reactions, nor centres oral to the abducens nucleus for those reactions in which the sixth nerve alone is concerned. These ocular reactions persist after ablation of the dorsal part of the mesencephalon and corpora quadrigemina, and when Forel's decussation is divided.

The volume is excellently reproduced and liberally supplied with figures which illustrate the nature and scope of the author's experiments.

Handbuch der Neurologie des Ohres. Herausgegeben von G. ALEXANDER, O. MARBURG und H. BRUNNER. 1ter Band, 2te Hälfte. Berlin und Wien: Urban und Schwarzenberg. 1924.

The first part of this volume was recently reviewed here; that under notice now completes the volume and is to be followed soon by the special part of the work in which all affections of the ear with neurological bearings and lesions of its nervous connections will be dealt with.

This part occupies nearly five hundred pages and is illustrated by more than two hundred illustrations.

The first article, by Alexander, is devoted to the pathology of the nervous portions of the auditory organs. A large part of this is mainly of otological interest, but the sections on the eight nerves and their peripheral ganglia, and on the anatomy of the diseases of the temporal bone which are associated with intracranial lesions, concern neurologists closely.

The next article is by Marburg on the general pathology of the central nervous system. Although his aim has been only to make intelligible the pathological states that will be described in the special part of the work, he has provided a remarkably concise compendium in which the chief ætiological factors in nervous disease are systematically classified, and the main types of pathological reaction of the cells, fibres and supporting tissues to disease are described.

The section on methods of clinical examination is opened by Cemach, who writes shortly on the value of the so-called cochlear reflexes in the diagnosis of real and simulated deafness. This is followed by a long article by Hugo Frey on the investigation of hearing; it will appeal chiefly to aurists, but should prove a useful introduction for neurologists to this important subject, more especially as it contains a critical summary of the value of the different methods and of the

significance of the results they yield. Brunner deals comprehensively with the symptomatology of disease of the vestibular nerves, including subjective symptoms as vertigo, anomalies in the position of the eyes and head, the different forms of spontaneous nystagmus and their pathogenesis, disturbances of balance and the methods of clinical examination of the labyrinths and the significance of the results they give. This article includes everything in the present state of our knowledge that may be necessary for clinical work and is followed, as all the sections are, by a very full bibliography which will enable readers to refer to the original papers which are quoted.

Ohm, in his article on the investigation of nystagmus, deals chiefly with the methods of graphic recording and the results they yield. The volume closes with a well-illustrated article by Schüller on the diagnosis of diseases of the ear by radiography.

A very complete index is also provided for the whole volume, which will add to the value of the work as a book of reference.

Handbuch der Neurologie. Begrundet von M. LEWANDOWSKY. Ergänzungsband, 1ter Teil, 2te Hälfte. Herausgegeben von O. Bumke und O. Foerster. Berlin: Julius Springer. 1924. Price 5.25 dollars.

The second half of the first supplementary volume of Lewandowsky's "Handbuch" extends to about 300 pages. It contains five separate articles, all of which are of considerable importance, for though they are mainly devoted to different aspects of war neurology and psychiatry, in which our interest can be no longer acute, they have collected some of the medical experiences of the late war which have added materially to our knowledge of local and general affections of the nervous system.

The first article is a long contribution by Pfeiffer to the psychical disturbances that follow war injuries of the brain. It is particularly distinguished by the elaborate methods of measurements and recording employed, and by the numerous tables in which the results are displayed. There are interesting chapters on the estimation of the capacity for work and on the results obtained by systematic re-education. F. Kramer's section on aphasia, aprasia and agnosia, is regrettably short, but contains a summary of the different views that have been put forward. Stertz writes on the psychical and nervous disturbances following general disease, infections and intoxications.

Lenz and Goerke contribute exhaustive articles on the symptoms of war injuries of the cerebral visual system and of the auditory nerve respectively. These are among the most interesting chapters of the whole volume and must be consulted by everyone who is interested in the neurological aspects of ophthalmology and otology.

Long bibliographies are appended to all the articles, but they include almost without exception references to papers by German authors only.

The Diagnosis of Nervous Diseases. By Sir JAMES PURVES-STEWART. Sixth edition. London: Arnold and Co. 1924. Price 30s.

Sir James Purves-Stewart's book is so well known, both in its English form and in the many translations that have been made of it into other languages, that it needs little notice here. The present, or sixth edition, has undergone considerable revision and has also grown in size, unhappily perhaps, for its increasing bulk has undoubtedly diminished its value as a reference book for the more elementary student and general physician, as the earlier editions professed to be. But it has at the same time become more systematic, and the greater attention that the anatomy and physiology of the nervous system have received in its successive editions, and the fact that, as in the rewritten chapter on the psychoneuroses, considerable space is devoted to the nature, etiology and pathology of disease, makes the present edition approximate more to the textbook class.

The arrangement of the matter remains however unaltered, and is possibly that best adapted to the author's purpose, which is to provide a volume in which the significance of any symptom can be easily looked up and determined. Otherwise there could be little excuse for grouping into one chapter and describing under the title "Tropho-neuroses" such diverse conditions as anorexia nervosa, acromegaly and perforating ulcers.

The chapter on the cerebrospinal fluid and the modes of obtaining and examining it is very complete for a book of this size; cistern puncture and pneumo-radiography are referred to, but it is regrettable that the significance of pathological changes in the fluid are not more fully described. A table or series of tables could have been usefully inserted here.

The book is well printed, and the numerous illustrations that distinguish it are excellently reproduced.

Colour Vision. By Sir J. H. PARSONS. Second edition. Pp. 323, figs. 94. Cambridge University Press. 1924. Price 25s.

Everyone who is familiar with the physiology of the eye will surely agree with the view that the study of colour vision is almost too intricate for those who are not specialists. The literature is so scattered, and the terms used have such carefully graded meanings, that a lifelong study is not excessive for the acquisition of really intimate knowledge.

It is for reasons such as these that the first edition of Sir John Parsons' book received such a hearty welcome. It is written by one who really knows the ins and outs of his subject, but one also who has the gift of describing each separate phase in a way which even the least learned can understand. The second edition is no less welcome than the first for the following reasons: It possesses all its good points, and at the same time contains much new matter. One example may be given, namely, the survey of Professor Frank Allen's experiments, which will be found on pp. 244 to 248. Here the author dis-

cusses what may prove to be the most important contribution to the study of colour vision of this decade. Not only are the methods employed novel (and it is new lines of attack that are badly needed at the present time), but the results themselves are of fundamental importance. It may perhaps be added that they form very convincing evidence in favour of the trichromatic theory of Young.

Fünfzig Jahre Neurologie. Von C. von MONAKOW. Zürich: O. Fussli. 1924. Price 5½ francs.

This small booklet contains two addresses given by von Monakow at the special meeting of the Swiss Neurological Society, held to celebrate his seventieth birthday last year.

The author compares himself to a climber who, after a long ascent has reached a peak upon which he can look back on the way he has passed, and at the same time see more clearly than he hitherto could the relation of his track to the surrounding country. Now, after fifty years in the study and practice of neurology, he looks back not merely on his own experiences, but on the growth of the science from a stage in which the neurologist was represented only by electro-therapeutists, and when even most of the methods which have advanced our knowledge were undreamt of.

But these addresses are not merely historical reviews, for the author's own views on the more important principles in the physiology and pathology of the nervous system, the lines in which he thinks further development can be most hopefully expected, and the more urgent problems that await solution, are all discussed in a concise yet easily intelligible manner. It is particularly these features which give the book its practical value as a guide to the younger workers by one who has acquired such a ripe experience and contributed so much himself to modern neurology.

The first lecture bears the title "Hirnpathologisches"; the subject of the second is "Die Neurosenfrage einst und jetzt." The one is devoted to the physiology and pathology of the nervous system, the second to the nature of the neuroses.

Leitfaden für die Untersuchung und Diagnostik der wichtigsten Nervenkrankheiten. Von A. STRÜMPELL. Leipzig: F. C. W. Vogel. 1924. Price 6 marks.

The professed object of this book is to provide students with a short introduction to clinical neurology, and to introduce older practitioners who have long ago left the teaching schools to modern methods of examination and diagnosis of nervous diseases.

The most interesting section is that in which the methods of examination are described; this is admirable and excellently adapted to its object. The next chapter deals with the symptoms of local disease of the spinal cord and brain, and the last with the differential diagnosis of the more common and

important nervous diseases. As might be expected from the pen of such a well-known and experienced teacher it is on the practically important points that most emphasis is laid.

Surgical and Mechanical Treatment of Peripheral Nerves. BYRON STOOKEY, M.D. W. B. Saunders and Co. 1922. Pp. 462. 217 illustrations, 8 in colour.

This book deals with most of the aspects of peripheral nerve lesions as they come under the notice of the surgeon. It is virtually a review of the work which has resulted from the war, and as such forms a useful book of reference. There is little or nothing original to be found in it, and perhaps the most useful feature is the copious bibliography which is given at the end of each chapter. It is to be regretted that the evidence of regeneration after nerve grafting is not examined and criticized. Had this been done it is certain that a less optimistic view would have been taken as to the possibility of obtaining a functional result by grafting. The material is well arranged in a readable form, and there are many useful illustrations.

Crime and Insanity. By W. C. SULLIVAN, M.D. London: Edward Arnold and Co. 1924. Pp. 256.

This is an authoritative work, written by a physician who has had very special opportunity of observing crime in its relation to mental disorder. The book is an expansion of lectures delivered to members of the classes of instruction in psychiatry organized by Sir Frederick Mott at the Maudesley Hospital.

The author, throughout his work, examines criminal conduct as it occurs in the different forms of mental disorder and mental defect. Each of the main clinical entities of mental disorder, as general paresis, senile insanity, dementia præcox, &c., has a chapter in which criminal conduct associated with that disorder is described and profusely illustrated with descriptive cases. There is a welcome infrequency of statistics and statistical graphs. Such figures as are given are clear, interesting and to the point. On the whole the crimes associated with the various mental states appear to be largely what the psychiatrist would expect. In general paresis for example, the characteristic crime is a foolish theft. Instances of murder occur as incidental to theft, or as a wild reaction to opposition or irritation. It will perhaps come as a surprise to medical men to learn that so many homicidal crimes occur in senile dementia. The chapters on Dementia Præcox and Moral Imbecility are of special interest in view of recent crimes which have aroused much popular interest. Dr. Sullivan gives a concise account of the history of the law in England with regard to criminal responsibility, and the McNaughten rules are clearly discussed. The author would like to see the law amended in regard to trials where an issue of insanity is involved. He would adopt a simpler test of

responsibility, and the admission of a qualified responsibility in cases where the offenders are abnormal, though not certifiably insane. Lastly he advocates the provision of an impartial and expert examination of the prisoner, the result of which shall be admitted as evidence.

Little can be said in criticism of this book, obviously the result of profound clinical and legal experience. Perhaps a later edition may include more modern psycho-pathological views. Every alienist should possess the work, and it may be recommended to practitioners, lawyers, and social workers.

Writers of "Original Articles and Clinical Cases" are supplied free of charge with 50 copies reprinted in the form in which the paper stands in the pages of "Brain." If reprints are required in pamphlet form, with wrapper, title-page, &c., and re-numbered pages, they must be ordered, at the expense of the writers, from Messrs. BALE, SONS & DANIELSSON, Ltd., 83-91, Great Titchfield Street, London, W.

Members of the Neurological Section of the Royal Society of Medicine can obtain the Index of "Brain" for the Volumes I to XXIII inclusive, that is, from its commencement to the end of 1900, from Messrs. MACMILLAN & CO., Ltd., St. Martin's Street, London, W.C., at the price of 6s. 6d., post free.

To those who are not members of the Neurological Section of the Royal Society of Medicine the price is 8s. 6d. net, and the volume may be obtained through any bookseller.

EDITOR.